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NEGLECTED DISEASES IN EAST ASIA: ARE PUBLIC HEALTH PROGRAMS WORKING?

HEARING

BEFORE THE

SUBCOMMITTEE ON EAST ASIAN
AND PACIFIC AFFAIRS

OF THE

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NEGLECTED DISEASES IN EAST ASIA: ARE PUBLIC HEALTH PROGRAMS WORKING?

WEDNESDAY, OCTOBER 6, 2004

U.S. SENATE,
SUBCOMMITTEE ON EAST ASIAN AND PACIFIC AFFAIRS,
COMMITTEE ON FOREIGN RELATIONS,
Washington, DC.

The subcommittee met at 2:36 p.m., in room SD–419, Dirksen Senate Office Building, Hon. Sam Brownback, chairman of the subcommittee, presiding.

Present: Senator Brownback.

OPENING STATEMENT OF HON. SAM BROWNBACK, U.S. SENATOR FROM KANSAS

Senator BROWNBACK. We'll call the hearing to order.

Thank you all for joining us today. Appreciate your being here.

The purpose of the hearing is to discuss ongoing efforts to control malaria and what the U.S. Government is doing, what the international community is doing, and what is taking place.

I am delighted to have Dr. Peterson here with us, and we will also have some testimony from other witnesses as well. Also, I want to note your personal service in the region, in Africa, as a physician and the work that you have done previously, and that is quite noteworthy and highly appreciated.

I was saying to Dr. Peterson before we started the hearing, this has really attracted my attention from the standpoint of the number of deaths and morbidity that has been going on due to malaria. This is something that we can deal with and I do not think we have dealt with effectively.

I want to go through a few charts that we have.

The burden of malaria: This disease is a huge killer and much more common than anything else that is out there. As I understand, it is the leading killer of children in Africa and third leading in the world.

If we compare what has taken place globally, we have got some charts to show some of what happened during the global eradication campaign years. When we used a very aggressive application of pesticide—in this case DDT—we had some very promising historical trends regarding what was taking place in treatment and dealing with the disease of malaria. This is a chart that shows global rates, and I do not think, Dr. Peterson, you can probably see the years very well, but this is 1900 here and it goes to 1990. We can see that when we really got aggressive on dealing with this and using all the tools available, particularly in this case, pes-

ticides, DDT, global rates went down aggressively. But they are spiking back up. The red line here, which is Africa, is spiking up aggressively, which to me is an area of great concern—that we see that rate jumping back up, where it has not shown a similar spike in other countries in Asia, Central and South American countries.

Here we see rates in some Asian countries. I have a chart up next that focuses on the same sort of thing. It shows much the same issue. These are Asian countries: Bhutan, Burma, Sri Lanka, India. We have got a rate here in 1965 to 1969 where there was aggressive spraying taking place, a multifaceted approach, very low infection rates, and then when that lost favor, the rates go up very high in these selective countries.

In South American countries, we show some of the same things. I have a comparison chart of 1960 to 1995. Here are the 1960's charts of malaria rates in South America. You can see the continent was really doing very well on infections on a per capita basis. By 1995, spraying is out of vogue, out of favor, and the rates go up dramatically in South America. This then puts, obviously, people there at much greater potential for their own harm, but also infection possibilities back into the United States.

The next chart. Resurgence is directly linked to DDT spraying or the lack thereof. As the number of sprayed households in South America increases, the excess cases over the amount seen during spraying exponentially increases. And this is just one of those inverse relationships where the numbers of cases were going down, but then when you stopped spraying, and the cases took off.

Even when DDT was being phased out internationally for agricultural use, Secretary Powell emphasized the dire humanitarian need for DDT to control malaria. We all know the difficulties of DDT and that the removing of it in this country is one of the things that brought the bald eagle back after numbers of eagles were down due to widespread agricultural spraying. But what we are talking about here is much more targeted spraying, household spraying, not the broad agricultural spraying that was used with DDT, that brought the weakening of the eggshell around the eagles' eggs that caused so much trouble here in this country.

But what we are talking about is a targeted spraying, to what the Secretary is referring, in recognition of the dire humanitarian need for DDT to fight malaria in Africa, an exception will be made for those purposes and should be. I think this is one of those cases where you have got a clear need and we have a targeted basis to be able to use it, and we can save a lot of lives.

But the WHO and other donors ignored this call. Some Asian countries and South Africa were able to keep spraying with DDT without those donor funds. They did it without donor funds, and we can see from South Africa's experience that Secretary Powell was absolutely right. Here we can see the South African model, what went wrong when they stopped DDT and the wrong medicine. Cases skyrocket. They said, we have got to stop. They went the other way. Cases of malaria go down.

South Africa had been controlling its malaria for years with DDT. Environmental activists pressured the government the following year to stop these measures, prioritizing hypothetically unproven environmental concerns over the many lives of tiny chil-

dren and moms. And we can see then what happens in that situation.

Again, I want to emphasize we are not talking about the agricultural use, widespread use of DDT. This is household spraying, very narrow, very targeted.

So the government reinstated DDT spraying, the effective drug therapy of the ACT drug, and its cases fell again. It is a tried and true approach to conquering malaria.

The donor community, which launched the Roll Back Malaria program, did not support these measures, the DDT and ACT drug measures. And since the Roll Back Malaria promise to reduce the malaria burden by half, the trend has actually gone in the other direction, and we have seen that take place now.

We have another chart. And we will provide all these to you as handouts, but I wanted to get them out and for those that were in attendance.

We can actually see the Roll Back Malaria campaign coming in and actually numbers have gone up. The Roll Back Malaria has failed. Millions of deaths have resulted each year since the Roll Back Malaria made its promise. Not only has the donor community failed to incorporate the proven DDT intervention, but they have refused to support effective treatments. In fact, today UNICEF is handing out pills that do not work to Sudanese refugees in Darfur. We all know the situation in Darfur. But to give them the medicines that do not work, I think, to me, is a double tragedy.

The USAID record is one, I am afraid, that is not that good. Many words have been said that we need to do things, but effective interventions have been few and the dollars have been, I do not believe, effectively targeted. You can see that AID has put forward statements that it wants to step its efforts up, but they have not included funding real interventions in suffering countries. It refuses to fund drug purchases that actually will work, is requiring Africans to buy the bednets, and is not supporting the use of DDT.

I do want to note a good story on this, though. The Global Fund is an exception to some of the trends we have seen of the public sector entities, like USAID and the Roll Back campaign. The Global Fund, after public pressure earlier this year, reversed its drug policy and it does support some DDT targeted spraying and is moving in the right direction.

I put this all forward because I look at this and I just think we are putting some money forward, we are putting some effort forward, but if we do not get the policy right on it, we are going to keep getting people dying of this and having morbidity as a result of malaria, which is something that we can handle in today's day and age. We are seeing the impact in Africa. It does not need to take place.

I do realize it will take some difficult political decisions because there is going to be a fair pushback from some activists that do not want anything to do with DDT and do not want these drugs used. Yet, if that is the effective way and we can get these trend lines going back in the right direction, I would urge us to do that with U.S. Government funds. I think you will find a lot of support here if the Government gets on programs that do work and we do get

these deaths and morbidity by malaria moving in the right direction.

We will have two panels today. We do have a series of votes this afternoon. I am hopeful we are going to be able to get all of this together and into the record. Dr. Anne Peterson is the Assistant Administrator for Global Health, U.S. Agency for International Development. That will be the first panel presentation. Then we have two expert witnesses that will be presenting afterwards.

I did have a staff member just come back from a conference in Africa, meeting with a number of recipient countries who were begging her that they be allowed—and they are getting funding from us and from other international groups—for that funding to go toward intervention strategies, use of pesticides and the application of pesticides, use of effective drug regimes, and not be used for technicians, conferences, experts. They want help actually putting the medicine in the hands of people, buying the medicines, and using the pesticides directly. They want intervention strategies, not technicians. They were really pleading with her and through her, with me, that they be helped on these effective strategies.

So, Dr. Peterson, I know you bring a lot of personal experience and knowledge to these issues and to Africa, and I hope that this is one where we can work closely to get on a policy track that starts reducing these cases of malaria instead of the continued growth.

Thank you for joining us today. I will take your full testimony into the record. You can summarize. You can present it, whatever you would like to do. But delighted to have you here.

STATEMENT OF DR. ANNE PETERSON, ASSISTANT ADMINISTRATOR FOR GLOBAL HEALTH, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT, WASHINGTON, DC

Dr. PETERSON. Thank you, Senator. I really appreciate your convening this important hearing. I get to talk very often about HIV/AIDS and not so often about malaria, and as I think you pointed out very nicely, this is an area that is out of control. It is growing and it needs the attention of Congress. So I am very pleased that you have convened this hearing and invited me.

You talked about the impact of malaria on the families, on women and children. I would add that we have a newly identified population that is at risk. Those who are HIV-positive are at much higher risk of dying of malaria because of their compromised immune system. As we are looking at the growth of malaria, we have a new and large vulnerable population that is getting larger by the minute. So coinfection is a big issue.

I appreciate your understanding of the issues and you have raised a number of very deep concerns that I hope I will begin to address, as I give my opening statement and in answering some of the specific questions for you.

We do know that most of the people who are affected are women and children. And the U.S. Government has been a leading force in the worldwide battle against malaria. Just this year we had $80 million for malaria. This is a four-fold increase over the past 4 years. This is the kind of scale-up that is necessary to begin to curb the kinds of trends that you have just shown to reach national

level impact instead of small-scale projects. We are moving toward better policies and visibly stronger programs. You talked about getting drugs into the hands of people, but also meeting that need based on strong policies. That is part of the leadership that the U.S. Government has been doing in the past years.

Seven countries, specifically in Asia, receive support for malaria with a major focus on limiting the emergence and spread of drug-resistant forms of malaria in the Mekong subregion of Southeast Asia, including Afghanistan, Cambodia, India, Indonesia, Philippines, Nepal, and Thailand.

We provide support to national malaria programs in 20 countries in sub-Saharan Africa where the burden of deaths is the highest.

The international experts have identified a policy of three priority interventions that together reduce the deaths of illness from malaria. There is not a single bullet. Because of the complex nature of malaria, its transmission, and the people at risk, you need a comprehensive package.

The first component of the package is prompt and effective treatment with an antimalarial drug within 24 hours of the onset of fever.

The second component is prevention of malaria through the use of insecticide-treated bednets for young women and children.

And the third component is provision of intermittent preventive treatment for pregnant women as part of their antenatal services.

Other parts of an integrated program, depending on the epidemiology and the mosquito characteristics, are indoor residual spraying and the use of insecticides and environmental cleanup.

We know that a comprehensive approach that includes prevention, an effective and prompt treatment, and research for better tools is the most effective strategy for saving lives. We have seen this in Asia with the recent emergence and spread of multidrug-resistant malaria. There has been a threat to reverse the gains that we have seen in malaria. We have been very concerned about this increase and invested significant resources into documenting the speed and the scope of the developing antimalarial drug resistance and the burgeoning deaths due to malaria.

Because of the cross-border nature of the drug-resistant malaria problem, surveillance and disease control capacity are needed in Southeast Asia. We have been supporting a coordinated approach since 1999, together with the World Health Organization, to monitor drug resistance. The U.S. Centers for Disease Control and Prevention have been a very close colleague in our efforts to do the surveillance. As a result of the drug resistance data, USAID, the other donors, and the national governments themselves can bring forward the appropriate policies and, in fact, have updated a number of the East Asian countries' malaria treatment policies. So again, the right policy is what is needed. You need to have the right data to make that happen.

The malaria programs in many of the Mekong Delta region now use combination therapy which includes the new artemisinin-based drugs. USAID has played a major role to change national malaria policy to ACT in three of the six countries in the Mekong region. We know from many infectious diseases that simultaneous use of multiple drugs instead of a single drug regimen slows the develop-

ment of resistance. In fact, a fair amount of the change in trends of malaria that you showed is due to increasing resistance and the fact that we had single drug regimen in the past.

The World Health Organization and Roll Back Malaria, including USAID, now recommend that all countries experiencing resistance should move from a first-line single therapy to combination therapy, ideally including artemisinin drugs. In fact, USAID is working in a number of countries to grow more of the plant from which artemisinin is derived in order to increase the supply of the artemisinin drugs.

We predict that there will be a need for almost 300 million treatments annually by 2008, and the majority of those drugs are likely to be needed in Africa. Therefore, it is very important to expand the production of the artemisinin.

We have also been working with global partners to increase the pharmaceutical producers to gauge their interest and willingness to scale up production. We have been working with financial institutions like the World Bank and the Global Fund to see if they are willing to mobilize sufficient support for financing of ACTs, and we have worked with the technical agencies to prepare countries for effective application of those resources.

We have been working with 11 of the East Asian countries that have received the Global Fund awards for malaria to make sure that the policies and the technical assistance that they need are in place to retrain the physicians, the health care providers, and the providers of the drug itself to be ready to move to the new drug regimens.

Just last week in Nairobi at a Global Fund programming meeting, USAID and HHS provided technical support to 25 recipient countries, including Pakistan and Indonesia, to pave the way for ACT introduction, including addressing drug management, policy reform, and appropriate use.

But we need to remember that even if we get ACTs out to all of the countries and if everyone uses them properly, malaria parasites can still grow in patients if we have poor drug quality or wrong formulations. Unlike in developed countries, poor quality medicines, either produced intentionally as counterfeits or accidentally because of poor quality control, are readily available on the open market and often are visually indistinguishable from the genuine product. USAID has been very involved in looking at the drug quality issue especially for malaria drug products. In one study in East Asia, 38 percent of artesunate samples from drug shops in Burma, Cambodia, Laos, Thailand, and Vietnam contained insufficient or no active ingredient. Other studies have detected other poor quality antimalarials, including chloroquine, mefloquine, and quinine.

Besides contributing to the drug resistance, which will exacerbate the trends in malaria, poor drug quality is equally dangerous for the individual patient. In 1999, at least 30 people in Cambodia died after taking SP, an older and less effective antimalarial drug, which was sold to them as artesunate. Poor quality drugs sometimes also contain toxic products that can be lethal.

USAID is strengthening national drug regulatory authorities. The aim is to improve the manufacturing of pharmaceuticals

through good manufacturing practices, including drug quality control in national programs. Across the Mekong Delta region, USAID provides support for 37 sentinel surveillance sites for monitoring drug resistance. These sites, the national malaria control programs, and drug regulatory authorities will be linked to create a regional warning system for poor quality drugs found in the market. USAID is also working to build similar sentinel surveillance systems in Afghanistan, Bangladesh, Nepal, and India.

Prevention, though, is still the key and use of insecticide at the household level is the mainstay of prevention. There are two main ways to administer insecticide treatment at the household level: Through indoor residual spraying, as you talked about, which was the centerpiece of the eradication campaign of the fifties and sixties, or through the more recent advent of insecticide-treated nets, ITNs. For those individuals at risk for malaria, ITNs are still the most practical and effective means for protecting the largest percentage of populations, and consistent use of ITNs has been shown to decrease severe malaria by 45 percent, reduce premature births by 42 percent, and cut all-cause mortality by 17 to 63 percent. In Cambodia, where malaria was a major problem among rural populations, with strong USAID support, a twin strategy of deploying ITNs and effective treatment reduced malaria incidence by more than 70 percent.

USAID does provide free nets and promotes targeting for heavily subsidized ITNs to the most vulnerable populations, pregnant women and children under 5, and the poorest populations. Nets can be deployed now in desperately poor countries where malaria-related deaths are highest and can be put into the hands of parents who want to protect their children instead on relying on government systems that, as you pointed out, in the past have not taken care of their populations.

The other way to bring insecticide into play in preventing malaria is through IRS, indoor residual spraying. Contrary to popular belief, USAID does support the use of DDT in its malaria control programs. We are fully supportive of careful use of DDT through indoor spraying of the interior walls. It has a potential role in malaria prevention in some countries in certain circumstances, but a global one-size-fits-all strategy that requires the use of DDT might be counterproductive.

Last December, I visited Ethiopia as they were responding to an unprecedented wave of malaria deaths. USAID was supporting Save the Children in the provision of both nets and indoor residual spraying. In the Cambodia example I just mentioned, they chose and were successful at turning around a malaria upsurge using bednets plus ACTs.

As we consider the plight of those who face these deadly diseases, we must act rapidly with the most effective methods of treatment and prevention. We must and are responding to this challenge, but I must emphasize that there is no silver bullet, no single intervention that is the answer to malaria. We must support a comprehensive approach that includes prevention, effective treatment, and research for better tools.

The session was to talk a little bit about TB, and I will just say that TB, like malaria, is on the upsurge. It has some of the same

problems of old drugs and too little attention for the scope of the epidemic.

Similarly, when we look at the child survival strategies overall, malaria is one of the major killers and we have great opportunities to do more in these areas of international health than we have been doing. USAID is spending a lot of time trying to prioritize where the scarce resources that we have can make the most difference for women and children. If we only have the resources before us, what are the biggest priorities? Where can we make the most difference with the interventions that we have, which are the most cost effective, and which will save the most lives? Public health is always about balancing competing goods, and in malaria, both in treatment and prevention, we have competing interventions, we have competing goods, and it is a balance for each country, for each place, and for each circumstance. It really needs a comprehensive strategy.

Thank you.

[The prepared statement of Dr. Peterson follows:]

PREPARED STATEMENT OF DR. ANNE PETERSON, ASSISTANT ADMINISTRATOR FOR GLOBAL HEALTH, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT, WASHINGTON, DC

Thank you, for convening this important hearing and for inviting me to testify on a very deadly disease, malaria.

Malaria affects the health and wealth of nations and individuals alike around the world. It is not only a disease of poverty but also a disease that causes poverty and is a major constraint to economic development.

As a public health physician who has worked internationally and domestically for more than 20 years, I am very pleased at the growing interest and response to the challenge malaria poses. The international community has mobilized funding and action recently to develop and implement sustainable actions against malaria. I will address the burden and suffering caused by malaria with a special focus on East Asia and outline what USAID is doing to save lives now and in the future.

Malaria

Worldwide, it is estimated that malaria kills more than one million people each year, making it the world's third deadliest infectious disease, after AIDS and tuberculosis. But malaria—spread by mosquitoes—is the most common of the three diseases, with more than 500 million persons experiencing acute malaria illness annually, compared with 5.3 million for AIDS and 8.8 million for TB. Each year there are about 3.6 million confirmed malaria cases and 6,000 malaria deaths in Asia and the Near East. However, there are probably many more unreported cases and deaths given that malaria occurs mostly in rural areas where health services and surveillance are weak. Malaria also accounts for a loss of approximately $12 billion a year in gross domestic product in Africa alone.

Eighty-five percent of malaria deaths occur in Africa, while about eleven percent of the deaths occur in Asia and the Near East. In Africa, malaria's greatest impact is felt by very young children and pregnant women because of their reduced immunity to the malaria parasite. As many as a quarter of childhood deaths in endemic areas of Africa are attributable to malaria. But infection of African women during pregnancy also takes a huge toll, both on the health of the mother as well as on the development of her unborn child. Placental infection in Africa is a significant contributor to low birthweight and subsequent neonatal death. In areas of unstable or epidemic malaria such as Asia, all persons are also at risk of serious illness and death. The drain on the physical and financial resources of households and communities of the disease, as well as the often ineffective attempts to respond to it, is well documented.

Scope of USAID Role in Battling Malaria

The United States is and has been a leading force worldwide in the battle against malaria. USAID has directed and supported critical research that forms the backbone of some of the most effective interventions, including insecticide-treated mosquito nets (ITNs), rapid diagnostics, and drugs. It is also studying ways to identify

and deal with increasing drug resistance. Our technical and financial resources are being brought to bear around the world and leveraged to increase global commitments to reduce illness and death. This year USAID committed over $80 million for malaria programs—a nearly four-fold increase since 1998 when USAID's Infectious Disease Initiative was launched. These new and expanded resources have allowed for a significant scaling-up of malaria activities to have national level impact and have led to increased coverage with interventions, better policies and visibly stronger programs. Many countries in Asia are also receiving support for malaria from the Global Fund to Fight AIDS, TB, and Malaria. I will say more about the Global Fund later.

Seven countries in Asia receive USAID support for malaria, with a major focus on limiting the emergence and spread of drug-resistant forms of malaria in the Mekong subregion of Southeast Asia. These include Afghanistan, Cambodia, India, Indonesia, Philippines, Nepal and Thailand. Activities supported are determined by local priorities, resource availability, and complementary activities by other donors and multinational institutions.

The international efforts to fight malaria are largely coordinated by a global partnership that includes leaders from across Asia, local health institutions, the World Health Organization (WHO), UNICEF, World Bank, UNDP, multilateral agencies, the Department of Health and Human Services (HHS), specifically the Centers for Disease Control and Prevention (CDC), international, national and local NGOs, and the private sector. USAID is a key partner in the Roll Back Malaria Partnership.

Integrated Flexible Program Approach Saves Most Lives

International experts have identified three priority interventions to reduce deaths and illness from malaria, each of which is backed by solid evidence of their effectiveness. These three interventions are consistent with USAID's priority areas for investment in malaria. They are:

1. Provision of prompt and effective treatment with an antimalarial drug within 24 hours of onset of fever;
2. Prevention of malaria primarily through the use of insecticide-treated mosquito nets (ITNs) by young children, pregnant women, and other high-risk populations; and
3. Provision of intermittent preventive treatment (IPT) for pregnant women as a part of the standard antenatal services—proper use of which can reduce overall child deaths by up to 30 percent and significantly reduce sickness in children and pregnant women [this one is not really a focus in Asia since little has been documented on malaria in pregnancy].

Other parts of an integrated program—based on appropriate epidemiology and mosquito characteristics—are:

a. Indoor Residual Spraying and use of insecticides, and
b. Environmental Clean-up to remove mosquito breeding sites.

The three interventions to reduce deaths and illness from malaria are internationally agreed upon and can be adapted to the local context depending on the needs and priorities.

Improving Treatment With Effective Drugs

Historically, national malaria control programs have relied primarily on monotherapy with drugs, such as chloroquine, amodiaquine, or sulfadoxine-pyrimethamine SP (Fansidar®). These are the first-line treatment for *Plasmodium falciparum* infections, which are responsible for the vast majority of deaths due to malaria. However, many of these drugs are no longer useful in Southeast Asia as well in other parts of the world including Africa because of widespread drug resistance among *P. falciparum* parasites. Malaria programs in many of the Mekong countries now use a combination therapy which includes one of the newer artemisinin-based drugs. In Cambodia, Indonesia, and Thailand, USAID has been supporting efforts to improve rapid diagnosis and treatment of malaria, particularly in poor, underserved populations or where the disease is reemerging. Although prohibited from providing assistance to Burma, USAID is providing support to non-governmental organizations (NGOs) in western Thailand to address malaria and other priority infectious diseases among Burmese migrants.

USAID Instrumental in Tracking Spread of Resistance—Documenting Need for Better Drugs

Like many infectious diseases such as TB, gonorrhea, and pneumonia, resistance to antimalarial drugs can develop and spread in areas where these medicines are not used properly or where their quality is poor. In Southeast Asia, strains of *P.*

falciparum have developed resistance over the past 20 years to multiple antimalarial agents and very few drugs remain effective.

Because of the cross-border nature of the drug-resistant malaria problem and the need for improved surveillance and disease-control capacity in Southeast Asia, USAID has been supporting since 1999 a coordinated, regional approach led by the World Health Organization to monitor drug-resistant malaria in East Asia and, more recently, in South Asia and limit its spread. The U.S. Centers for Disease Control and Prevention have also been involved in these efforts. As a result of drug-resistance data collected with the assistance of USAID and other donors and partners, malaria treatment policies have recently been updated in a number of East Asian countries including Cambodia and Thailand.

At the country level, USAID is working with national malaria programs to: Improve the diagnosis of *P. falciparum*; providing effective combination therapies to vulnerable populations; expanding the use of insecticide-impregnated mosquito nets to limit transmission of malaria and the need for antimalarial drugs; and monitoring drug resistance, drug-use practices, and drug quality.

Drug Resistant Strains Present Additional Challenges

East Asia and the Pacific include Burma, Cambodia, China, East Timor, Indonesia, Laos, Mongolia, Philippines, Thailand and Vietnam. Populations at risk for severe disease and death in East Asia include children, pregnant women, people routinely in contact with forested areas where malaria-transmitting mosquitoes live, and rural and mobile populations with limited access to health services. While improved access to prompt diagnosis and effective treatment has contributed to a decrease in the number of malaria deaths here over the past decades, the recent emergence and spread of multi-drug-resistant (MDR) malaria threatens to reverse these gains as treatments become more complicated and costly.

USAID has been instrumental in documenting the extent of the drug-resistance problem as well as studying the factors—such as poor drug use and poor drug quality—that are contributing to the emergence and spread or resistance. This information is critical for focusing interventions on priority areas in order to preserve the effectiveness of current antimalarial drugs that are safe and affordable. Only a limited number of alternative drugs are available if the current therapies fail and there is little economic incentive for new drug discovery and development, given its high cost and the fact that malaria predominantly affects the world's poorest nations. Newer drugs are also likely to be significantly more expensive which can limit people's access to them, especially in poor, rural communities. If steps are not taken immediately to address the root causes of drug resistance, these drug combinations will also lose their effectiveness in the near future.

Identifying Factors Contributing to Drug Resistance

There are two main factors that are driving the emergence of drug-resistant malaria in East Asia and elsewhere. They are: poor use of antimalarial drugs; and use of poor-quality antimalarial drugs. Both result in under-dosing which can allow malaria parasites to survive and adapt while exposed to sub-lethal amounts of the medicines. On the issue of poor drug use, health care providers and drug sellers can contribute to the problem in several ways, including: prescribing/dispensing the wrong drug when a patient has malaria; and prescribing/dispensing the proper drug, but in an incorrect dosage. Patients can assist the development of drug resistance by failing to complete the full drug course when they are ill. This may occur because they only had enough money to buy a partial treatment or because they stopped treatment once they started feeling better. Self diagnosis and medication can also lead to the wrong drug being used and/or the wrong dose. This occurs frequently as people go to traditional healers and drug sellers first before visiting trained health providers, especially if the official sources are not always stocked with the first-line therapy. Since prescriptions are rarely required for obtaining antimalarial drugs in the private and informal sector, patients have easy access to medicines. This may be especially common in international border areas where patients are poor and they may be avoiding the public health care system because they are in the country illegally or they do not speak the local language.

USAID has been instrumental in documenting the extent of the drug-resistance problem in the Mekong region, as well as studying the factors—such as poor drug use and poor drug quality—that are contributing to the emergence and spread or resistance. This three pronged approach in the Mekong is unique in allowing decision-makers to more broadly understand factors that affect community behaviors and to monitor their impact on drug resistance. Documentation of changes in drug resistance, quality and use will enhance the ability of countries to evaluate their national malaria drug policy and to introduce changes from a more informed perspec-

tive. This information is critical for focusing interventions on priority areas in order to preserve the effectiveness of current antimalarial drugs that are safe and affordable. A recent study of antimalarial drug use in western Cambodia revealed that only 11 percent of people who had malaria were using the recommended first-line therapy of artesunate+mefloquine, despite efforts by health officials to make the drug combination widely available through both the public and private sector. Moreover, 41 percent of people receiving treatment for malaria did not take the full course of the medicine. And 50 percent of people were self-prescribing with medications obtained in the private market.

Even if everyone in East Asia uses antimalarial drugs properly, malaria parasites can still be exposed to sub-lethal doses of antimalarial medicines if poor quality drug formulations are used to treat the disease. Unlike in developed countries, poor-quality medicines—either produced intentionally as counterfeits or accidentally because of poor quality control—are readily available on the open market and often visually indistinguishable from the genuine products. In one study in East Asia, 38 percent of "artesunate" samples from drug shops in Burma, Cambodia, Laos, Thailand, and Vietnam contained insufficient or no active ingredient. Other studies have detected other poor-quality antimalarial drugs, including chloroquine, mefloquine and quinine. Besides contributing to drug resistance, poor drug quality has real health implications for the individual patient. In 1999, at least 30 people in Cambodia died after taking SP (an older, less effective antimalarial drug) which was sold to them as artesunate. Poor-quality drugs can also contain toxic products which can be lethal if ingested.

Ensuring Drug Quality and Appropriate Drug Use

USAID is strengthening national drug regulatory authorities. The aim is to improve the manufacturing of pharmaceuticals through good manufacturing practices, including drug quality control in national malaria programs. At 17 sentinel surveillance sites in six countries in Southeast Asia and Africa, the United States Pharmacopeia Program (USP DQI) has trained staff of national malaria programs to collect and test drugs for quality, using low technology screening methods. Sentinel surveillance sites, national malarial control programs and drug regulatory authorities will be linked to create regional warning systems for poor quality drugs found in the market. USP DQI has also provided technical assistance in good manufacturing practices to selected producers of malaria drugs in Cambodia, Laos, and Vietnam. At the same time, USAID is also working with the Management Sciences for Health (MSH) Rational Pharmaceutical Management (RPM) Plus program to identify household and provider drug management and use problems, and to strengthen the capacity of local health officials and partners in East Asia to utilize this information to improve access to high-quality antimalarial drugs in the public and private sectors and to ensure their appropriate use. RPM Plus is also working with WHO and other partners to develop and implement a standardized methodology for monitoring the extent of ACT introduction as first line therapy in several Mekong countries.

Mainstreaming Rapid Diagnostics

New community-based approaches to diagnostics, including rapid diagnostics tests, can help overcome insufficient laboratory capacity or resources so that disease surveillance information can be rapidly used for action. USAID is working to develop diagnostics tests for both *P. falciparum* and *P. vivax* infections and assisting in mainstreaming their use around the world. In Southeast Asia, artemisinin-based combination therapies (ACTs) are routinely deployed with rapid diagnostic test kits so that these newer and more-costly therapies are used only when needed. USAID has also been supporting the development of quality assurance system to allow countries in East Asia to verify that their rapid tests are not degrading over time under normal field conditions.

Combination Therapy Recommended by WHO, Roll Back Malaria and USAID

We know from many infectious diseases that simultaneous use of multiple drugs instead of a single regimen slows development of resistance. The World Health Organization (WHO) and the Roll Back Malaria partnership (including USAID as one of the partners) now recommend that all countries experiencing resistance to their current first-line, single-drug therapy should change to a combination therapy, ideally including an artemisinin drug. The rationale for using combination therapy for malaria is similar to that for the treatment of tuberculosis, cancer, and HIV infections. When used alone, antimalarial drugs are more likely to select resistant parasites. The addition of a rapidly-acting and highly effective second drug, such as artemisinin or one of its derivatives, greatly reduces the probability of selecting parasites that are resistant to both drugs. This should prolong their useful therapeutic lifetimes. The WHO and Roll Back Malaria (RBM) recommend several ACT

options: artemether/lumefantrine (Coartem®) or artesunate plus either amodiaquine, sulfadoxine-pyrimethamine, or mefloquine. USAID has supported the development and critical research for ACTs.

Over the past year the RBM partnership has developed a comprehensive "roadmap" on how best to ensure access to and effective use of ACTs. The roadmap highlights major milestones and potential barriers towards achieving full access to and appropriate use of ACTs—and more importantly, establishes a framework for prioritizing the actions of the RBM partnership.

USAID and our global partners have worked with endemic countries over the past several months to assess their treatment needs. We are working with pharmaceutical producers to gauge their interest, willingness, and ability to scale-up production of ACT as well as with financial institutions to determine their ability to mobilize sufficient support for the financing of ACTs. We are also seeking help from development and technical support agencies to ensure in-country support for effective application of these resources.

We have identified four potential "bottlenecks" or barriers that hinder access to and effective use of ACTs:

- The capacity of agricultural producers to increase their yields of the plant *Artemisia annua,* the source of artemisinin;
- The number and capacity of pharmaceutical industry to produce high quality ACTs;
- The availability of resources to finance their procurement; and
- The availability of training and capacity to build support in country for widespread and appropriate use.

The identification of these potential bottlenecks in turn has led to an agreement within the RBM partnership of the key actions needed for their resolution.

Enhancing Production Quality and Capacity

Ensuring high quality and low cost ACTs requires an adequate pool of qualified ACT producers. Currently, there is only one pharmaceutical company which has been "prequalified" by WHO as a manufacturer of quality ACTs. USAID in 2004 and 2005 will continue to work with WHO to maximize the number of "prequalified" companies. USAID's support will target both upgrading the production capacity of pharmaceutical companies to meet WHO's standards for prequalification and will assist the WHO in expediting the evaluation process. USAID and its partners in Roll Back Malaria are currently working with legitimate local producers in Asia to assist them in incorporating Good Manufacturing Practices into their drug production facilities. This will help reduce the number of poor-quality antimalarial drugs available on the market, improve cure rates, and slow the emergence of drug resistance.

Financing ACTs

USAID and RBM partnership is taking a two-pronged strategy: (1) To identify financing over the next 18–24 months for country procurement of ACTs; and (2) to address the longer-term financing of ACTs. To meet the long-term demand, USAID has commissioned the Institute of Medicine to convene an expert panel to study options for funding ACTs from 2007 and beyond. This study has just been released and provides a clear and practical "roadmap" for the long-term financing of ACTs.

While recent public discussions of malaria treatment have largely focused on which drugs to use, the real challenge to providing effective treatment is in the "nuts and bolts" of delivering these drugs to those in need: Enabling policies must be in place; logistic and management capabilities need to be upgraded; health workers need to be appropriately trained and supported; and communities and households need to be knowledgeable and cognizant of appropriate services. USAID is working with partners in the public and private sector in all of these areas to ensure that effective, affordable, and safe antimalarial drugs get to the patients who need them.

With these and other similar challenges in mind, USAID is bringing the full weight of its technical and programmatic resources in support of those countries that have made changes in their policies to ACTs to ensure that they have adequate support in procurement and management of ACTs, training of health workers in diagnosis and use of ACTs for treatment of malaria, and mobilizing communities and households. USAID is also presently working with 25 Global Fund recipient countries—11 in East Asia have received GFATM awards for malaria—in preparing detailed plans for the introduction of ACT over the next year.

Prevention of Malaria

For those individuals at risk from malaria, insecticide treated nets (ITNs) are the most practical and effective means for protecting the largest percentage of populations. Consistent use of an ITN has been shown to decrease severe malaria by 45 percent, reduce premature births by 42 percent and cut all-cause child mortality by 17–63 percent. In most settings, ITNs are unquestionably the most effective way that families can protect themselves from malaria.

Free Nets to Those Most in Need

USAID promotes targeting free or heavily subsidized ITNs to the most vulnerable (pregnant women and children under five years) and poorest populations—thus ensuring economics is not a barrier to net ownership. For example, USAID support in Indonesia helped the Ministry of Health to respond to malaria outbreaks and distribute 95,000 long-lasting insecticide treated bednets which provided protection for approximately 500,000 people in high-risk malaria areas of Central Java, and in Bali, Aceh and Lombok.

New technologies now provide long-lasting nets and treatments that remove the necessity for retreatment. These technical developments, the product of committed commercial sector engagement with Roll Back Malaria partners, render ITNs even more affordable, more easily used, and more effective. ITNs also have an additional advantage. Studies show some protection of children who live nearby a net, as opposed to IRS where there is no added protection.

DDT

Contrary to popular belief, USAID does support use of DDT in its malaria control programs. We are supportive of careful use of DDT for malaria control through the spraying of interior house walls—Indoor Residual Spraying, or (IRS). DDT is only used for malaria control through this spraying method. The spraying of pesticides which may include DDT does have a potential role in malaria prevention in some countries under certain circumstances. A number of other insecticides can also be used for IRS, and are in many countries when those alternative insecticides are safer and equally effective. IRS, when efficiently conducted in appropriate settings, is considered to be as efficacious as ITNs in controlling malaria.

From a purely technical point of view in terms of effective methods of addressing malaria, USAID and others have not seen IRS as the highest priority component of malaria programs for many reasons. In many cases, indoor residual spraying of DDT, or any other insecticide, is not practical, cost-effective and is very difficult to maintain. IRS requires major infrastructure, including a high level of organization, geographic coverage, application personnel and financial resources, regardless of what insecticide is used. To be effective, IRS needs 80 percent community compliance. It is also more expensive in rural or peri-urban than in urban areas.

In most countries in Africa where USAID provides support to malaria control programs, it has been judged more cost-effective and appropriate to put U.S. government funds into other malaria control activities than IRS. However, in countries in which circumstances support the use of IRS (including DDT) USAID has funded and supported such malaria control programs.

USAID regulations (22 CFR 216) require an assessment of potential environmental impacts of supporting either the procurement or use of pesticides in any USAID assisted project, but if the evidence assembled in preparing such an environmental review indicates that DDT is the only effective alternative and it could be used safely (such as in interior wall spraying undertaken with WHO application protocols), then that option would be considered. The U.S government is signatory to the Stockholm Convention on Persistent Organic Pollutants (the POPs treaty), which specifically allows an exemption for countries to use DDT for public health use in vector control programs, as long as WHO guidelines are followed and until a safer and equally effective alternative is found.

The United States voted in favor of this exemption. For example, this exemption was used to spray DDT and other insecticides in South Africa when certain mosquitoes developed resistance to the major alternative class of insecticides, the synthetic pyrethroids. Such situations are relatively rare, however, and demonstrate the value of the provisions of the POPs Treaty, which restrict and document use of DDT, but provide for its use when appropriate.

Prevention of Malaria in Pregnancy

While preventing malaria in pregnancy is not a major focus of work in Asia, it is in Africa. Each year, more than 30 million African women become pregnant in malaria-endemic areas and are at risk for *Plasmodium falciparum* malaria infection during pregnancy. Most women live in areas with relatively stable malaria trans-

mission, where the major impact of infection during pregnancy is related to anemia in the mother and the presence of parasites in the placenta. The resulting impairment of fetal nutrition contributing to low birth weight (LBW) is a leading cause of poor infant survival and development in Africa. HIV infection diminishes even more a pregnant woman's ability to control *P. falciparum* infections. The prevalence and intensity of malaria infection during pregnancy is higher in women who are HIV-infected. Women with HIV infection are more likely to have symptomatic infections and to have an increased risk for malaria-associated adverse birth outcomes.

WHO has recommended intermittent preventive treatment (IPT) using the antimalarial drug, sulfadoxine-pyrimethamine (SP), as the preferred approach to reduce the adverse consequences of malaria during pregnancy in areas with stable transmission. Since more than 70 percent of pregnant women in Africa attend antenatal clinics, IPT provides a highly effective base for programmes through use of safe and effective antimalarial drugs in treatment doses which can be linked to antenatal clinic visits. The potential of IPT to attain high levels of program coverage and its benefit in reducing maternal anemia and LBW makes it a preferred strategy in sub-Saharan Africa. In HIV-negative pregnant women, two doses of IPT provide adequate protection, but a minimum of three doses appears to be necessary in HIV positive women. Outside of areas with stable transmission in Africa and in other regions of the world, while malaria in pregnancy is a risk for both the mother and fetus, there is no evidence that IPT is worthwhile.

USAID played a key role in supporting the original studies in Africa that documented the efficacy of IPT in preventing the impact of malaria on both HIV positive and HIV negative pregnant women and their offspring. Many countries have already changed their malaria in pregnancy policies. Currently, through a coalition of partners, USAID is assisting ministries of health in about 10 African countries to implement IPT and distribute ITNs as part of a package of health interventions at the antenatal clinic level. Over the last year this technical assistance has contributed significantly to revision of outdated policies in Senegal, Ghana, Rwanda, and Zambia and to increased implementation of revised policies in DRC, Tanzania, and Kenya. Among women attending antenatal services in Tanzania, delivery of intermittent preventive therapy has increased from below 30 percent to over 60 percent.

Expanding Global Network

Multilaterals, bilaterals . . . no one agency can do it all. Roll Back Malaria partners—leaders from across Asia, health institutions, WHO, UNICEF, World Bank, bilateral agencies, international, national and local NGOs, and the private sector are engaged in the fight against malaria. One "home-grown" partnership in East Asia is the Asian Collaborative Training Network for Malaria which focuses on training and information sharing. This organization was created by countries to deal with common issues related to malaria control. Both USAID and HHS have participated in the development of training strategies and curriculum development.

Global Fund

Through the Global Fund to Fight AIDS, Tuberculosis, and Malaria, USAID, HHS and international partners have come together to combine financial, technical, management, and other expertise to reduce the public health impact of malaria. Over the past three years, the U.S. government has contributed $623 million to the Global Fund, and has appropriated for a FY 2004 contribution of up to $547 million this year. USAID and HHS are presently working with 25 Global Fund recipient countries—11 in East Asia have received GFATM awards for malaria—some proposals specifically focus on drug resistant malaria and include efforts to address drug quality and drug management.

We have some of the best malaria experts in the world who have been requested to be on technical review panels for the Global Fund for malaria and USAID provides in-country technical assistance to assist in the development of Global Fund proposals. Strategically, there is a rapidly evolving partnership between the Global Fund and USAID's malaria program. With USAID providing critical technical "know how" and the Global Fund providing the resources for the procurement of key commodities for the prevention and control of malaria there is a growing optimism that malaria endemic countries can soon begin turning the tide against malaria.

Partnerships

These actors are playing unique roles—roles only they can perform due to their expertise, positions and responsibilities.

Research institutions and pharmaceutical companies can develop improved treatments and interventions to help protect us against malaria and its impacts. USAID works closely with the HHS, which, with USAID support, provides technical assistance to the World Health Organization and ministries of health in a variety of areas

related to malaria diagnosis and treatment, prevention of malaria in pregnancy, use of insecticide-treated mosquito nets (ITNs), indoor residual spraying (IRS), and monitoring and evaluation of malaria programs. USAID also provides funding to NIH for work on a malaria vaccine.

Community- and faith-based organizations and other NGOs extend deeply into many of the most rural areas, reaching societies and cultures to ensure health care services and malaria treatments and interventions get to hard-to-reach populations.

National governments have especially important roles to play with specific, attainable steps to reducing the impacts of malaria—steps that only they can take. The international donor community, in partnership with developing country partners, can ensure that technical and financial resources are allocated where they will be most effective.

USAID is committed to working with these important partners to turn the tide against malaria and other infectious diseases.

And with so many new partners, the coordination of our efforts becomes even more critical. This is as true among the U.S. government agencies as it is among our international partners, including the new Global Fund. Coordination efforts must occur at two levels: At headquarters and in the countries we are assisting.

Research

USAID has also targeted the creation of a vaccine for malaria. A vaccine candidate against malaria is currently being tested in Kenya and Mali where the disease disables or kills hundreds of thousands of people each year.

After initial safety trials in the United States, clinical trials jointly supported by the Gates Foundation, the Malaria Vaccine Initiative began last year in Kenya with a safety study on some 50 adults.

The tests showed that the vaccine was safe in adults in Kenya, so this year testing was extended to about 50 children aged 1 to 4 years. The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), is now working with USAID in testing the vaccine on some 40 adults in Mali to obtain safety data in a different epidemiological setting.

While ACTs are now effective, we know that won't last. Research on new and better drugs is absolutely critical and another important part of USAID's strategy. We are supporting Medicines for Malaria Venture (MMV) and WHO in new drug development.

Tuberculosis (TB) Background

Tuberculosis (TB) is an ancient disease. While a cure has been available for over fifty years, TB still kills more than two million people every year. Each day, nearly 25,000 people develop active TB and 5,000 die from their disease. Approximately one-third of the world's population or two billion people are infected with TB. According to the 2004 WHO Global Report on TB, in 2002 there were an estimated 8.8 million new cases of TB, of which 3.9 million were sputum smear positive (sputum smear positive TB cases affect the lungs, are the most infectious and therefore the most responsible for transmission of the disease (SS+) or "infectious" TB). In 2002, the global incidence rate (per capita) of TB was growing at a rate of 1.1 percent per year, and the number of cases was growing at 2.4 percent. Asia leads the world in terms of burden of TB—of the 22 high burden countries in the world today (accounting for 80 percent of the world TB cases), 11 are in Asia, including 4 out of the top 5, (India, China, Indonesia, and Bangladesh).

The global resurgence of TB has been fueled by increasing HIV/AIDS prevalence, inadequate public health systems, and emerging resistance to anti-TB drugs. Persistent poverty, crowded living conditions, and delayed diagnosis and treatment contribute to transmission of the disease.

TB threatens the poorest and most marginalized groups, disrupts the social fabric of society, and slows or undermines gains in economic development. An overwhelming 98 percent of the two million annual TB deaths—and 95 percent of the new TB cases each year—occur in developing countries. On average, TB causes three to four months of lost work time and lost earnings of 20–30 percent of household income. For families of persons who die from the disease, the impact of TB is even greater as about 15 years of income is lost due to premature death. In developing countries, the impact of TB on the family is even more important as TB generally afflicts the most economically active segment of the population between the ages of 15 and 54.

Treating TB Through the Directly Observed Treatment, Short-Course (DOTS)

Much progress has been made since The Stop TB Partnership (of which USAID is a member) was launched in 1998. The Amsterdam Ministerial Conference on Tuberculosis and Sustainable Development held in March 2000 established global tar-

gets of 70 percent TB case detection and 85 percent treatment success rates in SS+ pulmonary TB cases to be achieved by the year 2005 in the 22 High Burden Countries (HBCs). These countries together account for 80 percent of the world's estimated cases, and served to catalyze governments and donors to address TB.

The Stop TB partners and countries have endorsed The Directly Observed Treatment, Short-Course strategy as the most effective strategy available for the treatment and control of TB. The DOTS Strategy has five components: Political commitment; passive case detection among patients seeking care at health facilities and diagnosis using sputum smear microscopy; standardized short-course treatment with direct observation of therapy at least in the initial phase; assurance of an uninterrupted supply of high quality drugs.

The number of countries implementing DOTS increased from 112 in 1998 to 180 in 2002 and one high burden country (Peru) reduced TB incidence sufficiently to graduate from the list of 22 HBCs. The Partnership has grown to include over 200 donors, nongovernmental organizations (NGOs) and other institutions, which demonstrates the strong global commitment to combat TB and to collaboration in that effort.

However, recent analysis of global TB trends and progress in DOTS implementation indicates that without an acceleration of DOTS expansion and program strengthening, these global targets will not be achieved for many years to come. Reported global DOTS coverage of 69 percent masks the reality that many people, even in areas where DOTS is reportedly available, lack true access to DOTS. While the overall treatment success in DOTS areas is 82 percent (2001 cohort) about 31 percent of the world's population resides in non-DOTS areas where treatment success averages just 40 percent.

USAID's Response

USAID currently supports programs to expand and strengthen DOTS in 34 countries worldwide, including eight in Asia—Afghanistan, Bangladesh, Cambodia, Egypt, India, Indonesia, Pakistan and the Philippines. Illustrative activities supported in these countries include training of health personnel, strengthening of laboratory services and provision of laboratory equipment, development of guidelines and training materials, and technical assistance to strengthen program planning, monitoring, evaluation, and supervision.

For example, in India, USAID has been a major supporter of the very successful national TB program—where DOTS coverage reached 71 percent of the population by the end of September 2003—774 million people. The death rate among TB patients nationally has dropped to less than 5 percent. In Indonesia, which is another of USAID's major TB programs, USAID has provided critical support to the expansion of DOTS in two major provinces, and provided the technical support for the national TB program's implementation of a Global Fund grant for TB. In the Philippines, USAID is not only providing critical support to the national public sector TB program, contributing to a 10-percent increase in coverage but has pioneered an innovative private sector program. This program is designed to ensure that private sector services follow appropriate regimens and are coordinated with the public sector. This is critically important in a place like the Philippines, where people with TB symptoms are more likely to seek treatment from private providers than from the public sector.

USAID's Technical Leadership

In addition to our direct support for improving TB treatment programs at the country level, USAID also provides assistance to support DOTS programs worldwide through several global mechanisms and partners such as the STOP TB Partnership and the Global TB Drug Facility (GDF). USAID is actively involved in the STOP TB Partnership—the Agency is a member of the Partnership coordinating board and USAID technical personnel are members of all STOP TB technical working groups.

The Agency provides funding and technical support to the GDF, and we are the second largest donor to the GDF. Since it was launched in 2001, the GDF has raised and committed $39 million for grants for anti-TB drugs. Through the GDF and USAID's technical assistance programs countries and NGOs also receive technical assistance and training to strengthen the management of anti-TB drugs. They can also purchase anti-TB drugs through the GDF direct procurement mechanism, and therefore take advantage of the highly competitive pricing and good quality products that are available through the GDF.

In this respect, the GDF is a perfect partner to the GFATM. Using funding provided by Global Fund grants for TB, countries and organizations can purchase TB drugs through the GDF direct procurement service.

Battling Multi-Drug Resistance

USAID is also working to address the problem of multi-drug resistant TB (MDR TB). We support country surveys to measure the magnitude of TB drug resistance as part of the on-going WHO/IUATLD Global Project on Anti-TB Drug Resistance Surveillance. To date, USAID has supported surveys in 15 countries or sites (including 3 provinces in China), with studies in 16 more countries ongoing or planned (including Indonesia and India). We also support an effective response to MDR TB by funding DOTS Plus for MDR TB pilot projects in a number of countries and settings, focusing on countries with the most serious MDR TB problem such as Russia (Orel and Ivanovo oblasts), and the Baltics (Latvia, Estonia, and Lithuania), and Kazakhstan. We provide funding to support the work of the STOP TB Green Light Committee (GLC). The GLC provides technical assistance and monitoring of DOTS Plus for MDR TB pilot projects. So far, the GLC has approved DOTS Plus pilot projects in 11 countries and another 14 applications are under review. DOTS plus projects that are approved by the GLC are eligible to purchase second-line anti-TB drugs at lower prices than on the open market. Finally, we support a network of supra-national reference laboratories that provide the necessary quality control for anti-TB drug susceptibility testing, and we are supporting training and operations research in hospital infection control to help reduce the risk of transmission of MDR TB in clinic or hospital settings.

USAID and Global Fund Support

USAID missions work closely with the Global Fund to Fight AIDS, TB and Malaria (GFATM) by leveraging mission funded programs with the substantial funding provided by the GFATM. USAID missions participate in the Country Coordinating Mechanisms, assist with grant proposal writing, and help countries prepare implementation and monitoring and evaluation plans for these grants. Through USAID technical partners such as the TBCTA and others, USAID missions provide support for technical assistance, capacity building and monitoring and evaluation to help the grant-recipient countries to effectively implement and manage GFATM grant-funded programs and activities. A total of $422 million has been awarded to 21 countries in the ANE region for TB control.

Investing in Disease Detection and Control

Drug-resistant malaria and tuberculosis are just two examples of the many public health problems that exist in East Asia. However, the basic approaches just mentioned—including capacity building, partnerships, developing new tools—also apply to other infectious diseases as well. As you know, East Asia has been in the spotlight over the past few years with outbreaks of new diseases including SARS and bird flu. While their mortality has been relatively low compared to diseases such as HIV/AIDS, TB, and malaria, these new diseases have had a major economic impact on trade, tourism, and foreign investment. First-response organizations such as the World Health Organization and the U.S. HHS have been providing key support to track these epidemics and identify ways to limit their spread and impact. In addition, USAID's Office of Foreign Disaster Assistance has provided emergency assistance to affected countries. As part of longer-term development efforts, USAID is also working to strengthen human and institutional capacity in disease surveillance and response so that new diseases can be rapidly detected and stopped before they spread widely.

Next Steps

There is much to do. If we are to meet our goal of halving malaria by 2010, and of achieving global program targets for TB, all of us, our esteemed partners from Asian governments, health institutions and our global partners must act together through the opportunity offered by the Global Fund and through the Roll Back Malaria and Stop TB partnerships at all levels, most importantly in countries, to deliver the tools we have in hand, to develop new tools, and to fulfill the promise of coordinated and concerted support to countries.

Senator BROWNBACK. Thank you, Dr. Peterson. I will go through a series of questions, if I can, with you.

Could you put that chart back up that showed the number of deaths by malaria just over a period of time? Did you get a chance to look at that or was it up too fast for you? Do those track with your trend lines? They may not be with the exact numbers, but do they track with your trend lines? Are we seeing a big increase in malaria infections and deaths in Africa?

Dr. PETERSON. I think those do track. In fact, in accordance with the worldwide eradication initiative, we truly hoped in the fifties and sixties that we would be able to eradicate malaria. We made huge progress, as you show, but the single intervention using one modality did not work. We were not able to completely eradicate malaria, and if you do not eradicate it completely, as we are seeing with polio right now, then it can begin to surge up again. So we could, and should, expect that if we do not continue to work at a communicable disease, we will see it come back.

And what has happened is not just whether there has been spraying with DDT or not or whether it could have been completely eradicated. We were not successful in the fifties and sixties using only the insecticide.

Senator BROWNBACK. But you really drove that thing down.

Dr. PETERSON. We did.

Senator BROWNBACK. And let us get the South African chart up there. You tell me where the analysis is wrong on this. South Africa said, OK, I will agree with you, we will stop using DDT, we will go with your drug regime. Their deaths and incidence of malaria skyrocketed. They said, OK, we are backing away from this stuff and we are going to go back to what we know worked, which is, we are going to use DDT. We are going to use a particular set of drugs. A dramatic fall, a dramatic fall. It looks like to me we have tried this a couple of times. We pretty well do know what the silver set of bullets are. I mean, there are a couple of them here. They have got to be used in tandem, and used in tandem, you can drive those numbers down hard and fast. It just seems like we are not using the set strategy that we know will work.

Dr. PETERSON. What you will see in South Africa is that they use two strategies. They used DDT and an effective drug treatment. And that is really what we are talking about, that you need to use more than one strategy. The reason we were not successful in the fifties and sixties is we had a single intervention. What we realize now is that when we do treatment, we need, whenever we can, to use more than one drug at a time to stop drug resistance. In fact, that is where a lot of the upsurge has happened, because we have had developing drug resistance over the last 20 to 30 years.

The issue is not: DDT or not DDT. It is: What is the most effective way to use insecticide to reach the greatest number of people? It can be DDT or it can be another insecticide, and it can be through spraying or it can be through bednets. They both have their place, and there are different reaches with the different modalities. The important thing is to be able to use the prevention strategies, the right one for the right place, and the treatment strategies and bring them both forward together in an integrated package.

Senator BROWNBACK. OK. Then why are we not doing that?

Dr. PETERSON. We are.

Senator BROWNBACK. Why are these numbers doing this on these other cases in Africa then? If we are doing it right, why are these numbers going up?

Dr. PETERSON. South Africa is a country with a small amount of malaria, mainly in circumscribed areas. It has a lot of funding itself, and it is using an integrated package. And it has done very

nicely with a good push of resources and an integrated package to take care of a small epidemic.

Other parts of Africa don't have the infrastructure to do national level indoor spraying, like South Africa has done, and they have much larger burdens of malaria in much more impoverished countries. So you are talking about a much greater scope of work in a country that has less capacity.

So we are doing the right things and we are making a difference. We have seen in places where we have changed the drug treatment policy, where we are doing programs for treatment of pregnant women, that we can bring down the death rates and the impact on children. We do not have the resources to do programming in all of the countries at national scale. This is where you will begin to see a change as USAID funding has gone up in the last 4 years. That is a very short period of time.

Senator BROWNBACK. Well, it takes a year on this. You saw that South African program.

Dr. PETERSON. Yes.

Senator BROWNBACK. Let me ask you this very directly on it. You have got $80 million, is what you have said, in your budget. Does any of that go for indoor spraying of DDT?

Dr. PETERSON. Yes. We are supporting indoor spraying in five or six countries.

Senator BROWNBACK. Do you know how many dollars you are putting into that? And are you providing the money to buy the DDT? What are you providing?

Dr. PETERSON. Usually, we have been providing the training and the assistance for the programs to go forward. You have to train the people. You have got to provide the logistics systems and put it together with the rest of the program.

Senator BROWNBACK. Is that what you are funding then?

Dr. PETERSON. Yes.

Senator BROWNBACK. So you are not buying DDT.

Dr. PETERSON. To my understanding, we are not buying the DDT, but we generally work in partnership with the countries and with our local partners. So the Save the Children Program that I mentioned in Ethiopia was being funded by USAID, but we did not actually buy the DDT ourselves. But it did include indoor residual spraying with DDT. It has included bednets to 50,000 women and children.

Senator BROWNBACK. Zambian health officials reported to my staff that they have repeatedly asked USAID for DDT funding for spraying and repeatedly been refused in that effort.

I do not want this to be a gotcha hearing. What I want to do is work with you. I look at these numbers and they make me cry because this does not need to be this way. In the world today, if we were able to drive those numbers like that in the fifties and sixties, we know how to do this. I want to make sure if we move forward on this—and I think we will, and we have tried to get some additional funding in this appropriation bill for malaria. It would be nearly double what you have now—that we are not scared of DDT. I understand the problem. I come from a farm background. I am used to using pesticides. I understand both the good and the problem with it.

The bednets I can see some usefulness, but also you cannot be under that net all night long. If you have got to get up and get around to get something or go to the bathroom, you are out from under the net. Mosquitoes are still around. I think it can work and be helpful.

And we are getting complaints that we are not supporting the effective drug strategy, but rather we are supporting cheaper drug strategies on this.

If we could, what is your breakdown of how the $80 million is being spent? Can you put it in categories for me or do you have that available to you now?

[The information requested was submitted and has been made part of the committee's permanent record.]

Dr. PETERSON. I do not have that available. I can get it for you. I will say that it includes research in new malaria drugs, research on vaccines, the surveillance, the assistance in policy change, and we have been actively moving countries to the new drugs. It includes this partnership with the agricultural sector to grow more of the new drug so that the supply will be available as we scale up the programs. It includes the training of people to use new medicines, to know that they should be integrating it into their pregnancy programs, and to begin to put malaria programs into our HIV/AIDS programs. Those are the kinds of things that we are doing, including moving whole countries from a policy of one drug to the more effective combination drugs.

As we look at the insecticide, we are not afraid of using the DDT. But it is very clear that there are places where it works better. If you are in an urban setting or a peri-urban setting where people are close together, it is much easier to go from house to house to house and do the spraying. But in the far rural reaches of any State in the United States or any country that we are talking about where people are spread out, then teams going from house to house, having to revisit houses because people are not home, takes more time, more money, and more teams to reach them. That is why having both modalities is so important. When you use the bednets, they can go out through normal commercial sector routes like Coca Cola, like flour and sugar go out, and it is available to the families where they can reach them. If we are relying on government sector infrastructure, it will work better in places where people live close together in areas where malaria is upsurging, where you go in for a short-term need.

What we really need to do is have the flexibility to address the epidemic, as it is changing, and deal with each country's needs, which will be different. South Africa is very different than Zambia, than Uganda, or than Cambodia. And we need to bring all of the modalities, not limit ourselves to just one.

Senator BROWNBACK. Are you considering in your current funding that you have, purchasing DDT or direct purchases of DDT by your recipients to distribute it? Are you considering that in your expenditures right now?

Dr. PETERSON. We certainly can consider it. We also are a major funder of the Global Fund, and I sit on the Global Fund board. The moneys are going for malaria in all of these different countries, which as you pointed out, are purchasing DDT. They are also the

major purchasers of the drugs themselves. That is U.S. dollars leveraging other donors to buy commodities and drugs. And so our bilateral programs really serve a unique purpose. When I meet with other donors, often U.S. Government—our bilateral programs are the only ones still providing technical assistance on policies, on how to make things happen, on how to get drugs from one place to another.

Senator BROWNBACK. So you are not considering it. You could, but you are not currently considering purchasing DDT by USAID funds.

Dr. PETERSON. We could consider it. I think the role that the U.S. Government is playing in our bilateral foreign aid programs is a special role. When we go and help countries get to the right policies or do the technical assistance——

Senator BROWNBACK. I understand that point. I am really trying to get to a narrow point here and then to understand why it is that you are not, when you acknowledge this is an effective strategy. It is a good strategy. It is part of the strategy, but we are not funding it. I want the other funds to do that and we are just going to provide technical assistance or bednets. If that is the deal, OK, that is the deal. I do not agree with it, but I just want to really try to understand why, when this is such an effective part of the strategy, we are not funding it.

Dr. PETERSON. Because, I think we have another mechanism that the United States is participating in, through the Global Fund and our other partnerships, that is set and ready to buy large amounts of commodities. What is unique about our bilateral programs that the other donors are not doing, is the assistance to make those programs work. The Global Fund is a financing institution and it is buying the commodities. Forty-five percent of what they are buying is commodities, including malaria treatments and DDT. They are having trouble making it work without our assistance.

Senator BROWNBACK. I understand that point and I appreciate it.

I want you to know we are receiving complaints about that; that these countries do not want the sort of things that we are funding; that I am getting. We can provide you names. Here are people who are saying, "look, I do not need another conference. I do not need another technician. I do not need another contractor. I need these drugs and this spray." They are willing to do it on their own in their distribution systems and the way they will go at it.

Obviously, we were able to figure out in the past how you could get some of this stuff distributed, at least the sprays and some of the drugs, where we drove this thing down so hard, so fast, in the fifties and sixties where your distribution problems would have been infinitely more difficult than those now in more remote areas.

I will look more at here, why we are just providing technical assistance in these areas rather than these items. I will look at it, and then maybe we need to respond here by saying, OK, then we need to fund the other programs rather than this one because that is where we actually get the delivery of the goods that the countries are asking for to actually drive the numbers down. And we can do that. We can go that route.

Dr. PETERSON. We have not heard these complaints from the countries. We would be very pleased to hear any specifics that you

have. We try and always be responsive to the country's needs, their decisions, and the route that they would want to go.

I often get ministers of health or ministries saying, please, would you just give the government the money or just buy us this. And when I say, well, does that mean you do not want this group providing this technical assistance to help you with your policies, they say, oh, no, no, we do want that and you are the only one still providing it for us. So I am happy to respond to specific country issues, but I often find that when they have to have a choice between what we are currently providing and something else, what they really want is both.

Senator BROWNBACK. I would like, if you would, for you to provide to the committee your breakdown of how you are spending the current allocation of funds.

I appreciated your hitting on tuberculosis. At another time, I would like to catch you more on other disease issues in developing countries and get from you your list of top five, top ten. I think we are hitting pretty hard the HIV/AIDS issue and are starting to be effective, and we are putting in billions on that. We have really stepped up. The administration, the President, has pushed this. It has been a great initiative. So they are really hitting strong.

My focus is to say, OK, what is the next level of issues that are there that we have not effectively addressed and we have not put near the focus on and let us start looking at that series of items. So we would like it if you could provide, when you get back, your top five or ten. Here are the ones that I am most concerned about and they do not gather as many headlines.

Do you have on the top of your head on what you focus on your top three or four that you believe, OK, these are the ones, if you would give me resources, that I would focus on?

Dr. PETERSON. AIDS, TB, and malaria are sort of the ones that have captured most of the attention, and we have touched on malaria and a little bit on TB today. But I think the equivalent area like malaria and TB, where we were making some great progress and have not done so well in the past, probably because we are focused on these other three diseases, is the child survival package of interventions. We still have 11 million children who die every year, and we could prevent probably two-thirds of them. We could prevent almost 7 million deaths. Malaria is one of the big killers within that group, but it is also diarrhea, pneumonia, malnutrition, and the vaccine-preventable diseases. Those are all things that we are working on but we are not making progress anymore. They are cheap. We know what works and we just need to do them at scale. So child survival is an area to balance with AIDS, TB, and malaria priorities. We talk a lot about HIV/AIDS, but in fact, it is the children who are orphaned by AIDS who are now dying of malnutrition and pneumonia and malaria because they are the most impoverished with the least access to the services. So that is my number one area of concern.

And within each country, it is a little different spectrum of what their needs are for that country. Cambodia is different than Ethiopia, two of the top countries for child survival problems. But that would be my other one, packaging the priority interventions by country needs.

Senator BROWNBACK. Well, thank you very much. If you have a chance, I would appreciate it—and I do not know if you can—if you would stick around to hear, at least, the presentation of the next two presenters. I think they are pretty thoughtful on this. Hopefully then, we will all be able to work together toward what we can see as effective strategy. I do appreciate both your public and private service because you have done this before in a private setting, and I appreciate that and I appreciate your doing it in a public setting.

Dr. PETERSON. Thank you very much.

Senator BROWNBACK. Thank you.

The second panel will be Dr. Donald Roberts and Dr. Robert Desowitz. Dr. Roberts is a professor of tropical health at the Uniformed Services University for the Health Sciences. He has conducted extensive international research on malaria. He currently operates an NIH-funded research program focusing on developing chemicals to replace DDT for preventing the spread of malaria.

Dr. Robert Desowitz is a renowned researcher, lecturer, and professor. He has published numerous books and articles, including "The Malaria Capers: Tales of Parasites and People." Dr. Desowitz has held faculty positions at universities around the world, including Singapore and Nigeria. He is currently professor emeritus of tropical medicines and medical microbiology at the University of Hawaii, and an adjunct professor of epidemiology at the University of North Carolina at Chapel Hill.

I am delighted, gentlemen, that both of you could be here to join us today with your expertise and background. I appreciate your testimony. Your written statement will be included in the record. If you would like to summarize, that would be fine. So, whatever route you would like to take. Dr. Roberts, let us start with you.

STATEMENT OF DR. DONALD ROBERTS, PROFESSOR, DEPARTMENT OF PREVENTIVE MEDICINE AND BIOMETRICS, UNIFORMED SERVICES, UNIVERSITY OF HEALTH SCIENCES, BETHESDA, MD

Dr. ROBERTS. Thank you, Chairman Brownback, for the opportunity to present my views on malaria control today.

Asia does not present us with the worst of malaria control problems, but this does not mean that there are no problems of malaria control in Asia. As you will see in my written testimony, conditions in many Asian countries are far worse today than they were decades ago when a systematic approach to indoor spraying of insecticides was used to combat malaria. The return of malaria to the country of South Korea is symbolic of the reversals that have occurred in the global strategy to control malaria. However, the malaria problem in South Korea is more than symbolic. There were 115,000 cases in North Korea in 2001, and malaria now poses a risk to our military.

The malaria control community around the world is presently locked into several different debates on best practices for dealing with a continuing and, in some areas, a worsening problem of a very preventable disease, which is the topic of today's meeting, and that is malaria. One part of the debate is whether to use insecticide-treated nets as the only preventive measure or to use nets and

indoor spraying of small quantities of insecticide on house walls. Real differences exist between these methods. Nets protect only those under the nets, whereas indoor spraying protects all within the household 7/24. The option of using one or the other is an important debate. If the decision is to go with nets alone, then public funds will continue to be used to pressure countries to abandon their uses of indoor spraying.

In a larger context, I am surprised that we have this debate at all. There is no scientific basis for stopping or preventing indoor spraying. On the contrary, replacing indoor spraying with nets defies a fundamental lesson of preventive medicine. Clearly delineated within the annals of occupational preventive medicine is the fundamental truth that the least desirable preventive measure for reducing environmental risk is reliance on personal protective measures. We have certainly learned this lesson over and over again in the military. This principle is expressed in the form of patients failing to take a full course of drugs, failure of troops to properly wear uniforms to prevent insect bites, or failure to properly apply topical repellents, or failure to use their bednets.

It is also a fundamental truth that proper use of nets requires user compliance. The user must be educated on the proper use and must then be highly disciplined in proper use night after night. Additionally, the user must be conscientious and follow a routine of repairing those nets and retreating those nets with insecticides. If we could be certain that there would be full and proper user compliance, we would still need to determine whether the practice would truly deliver a meaningful level of disease prevention. Let me present one single study to illustrate why we should worry about that specific issue.

A bednet study was conducted in the small and highly malarious Phan Tien village in southern Vietnam from 1995 to 1999. Case treatment and net use was supervised and monitored. Malaria was reduced but rose again in the last year. The investigators stated that after malaria was reduced, the population lost interest in the intervention. Basically after 5 years of costly effort, malaria in the last year had declined only 2 percent from numbers of cases in the beginning year. While this is not the best that we can expect, it certainly indicates that in the long term disease prevention can be very low indeed.

To repeat, the fundamental lessons of occupational preventive medicine is that use of personal protective measures is the least desirable of methods for reducing environmental risk. The flip side of this principle is that the most desirable method for reducing environmental risk is to engineer risk out of the human environment. The use of indoor spraying is absolutely consistent with that fundamental principle of preventive medicine, and let me explain why.

Most cases of malaria are acquired inside houses. Mosquitoes that aggressively enter and bite indoors transmit the infections. Indoor residual spraying can act to prevent mosquitoes from entering houses in the first place. If they still enter, then chemical contact indoors can cause the mosquitoes to exit without biting. If they remain indoors, the chemical can, with longer contact, kill the mosquitoes. In other words, the chemical applied to house walls exerts

multiple and sequential actions to prevent indoor transmission of malaria and other diseases.

These relationships explain why indoor spraying has been so wonderfully effective in combating malaria and other diseases. I want to emphasize that lack of effectiveness is not the reason that the World Health Organization and bilateral and multilateral donors have pressed countries to stop spraying programs. To the contrary, indoor spraying has been and continues to be the most highly effective preventive measure yet discovered for preventing malaria.

WHO, USAID, and others argue that spraying should not be used because it requires a strong and well-developed public health infrastructure. I would respond to that assessment by saying that spraying was used to reduce or eliminate malaria in many countries of the world long before WHO defined the organizational structures needed for indoor spraying programs. The countries accomplished these great achievements on their own. I can think of two remarkable examples. One is Guyana and another is Taiwan. Guyana began experimenting with indoor spraying in 1946. In that year, the country instituted a national program of spraying and reduced their malaria problems by 99 percent in 3 years, and they used no therapeutic drugs. Malaria treatments were not part of that program. Taiwan began a national program in 1952 and had reduced numbers of cases from 1.2 million cases to 676 in 1956. In comparison, during the last 20 years, treated nets have been pilot tested in many, many countries. There is not one result from those studies that can compare with the performance of indoor spraying of DDT in Guyana or Taiwan.

The statement was made earlier that countries have failed to protect their populations, and for that, they need to have training and encouragement to do so. The fact is that many of these countries have been pressured to stop those programs, and your graph shows the results of the pressures to change those programs.

To sum up my oral testimony, during the last 24 years, many developing countries have been pressed to stop programs of indoor spraying due to an environmental ideology that strives for an environmental utopia, an environment free of manmade chemicals. This ideology is strong and pervasive. It prioritizes scientifically unfounded risk of environmental harm over the basic health needs of the world's poorest and most vulnerable people. Countries need the freedom to return to the use of indoor spraying if they so desire. Today, due to pressure from WHO and bilateral and multilateral donors, developing countries really do not have that freedom.

Thank you.

[The prepared statement of Dr. Roberts follows:]

PREPARED STATEMENT BY DONALD R. ROBERTS, PH.D., PROFESSOR, DIVISION OF TROPICAL PUBLIC HEALTH, DEPARTMENT OF PREVENTIVE MEDICINE AND BIOMETRICS, UNIFORMED SERVICES, UNIVERSITY OF THE HEALTH SCIENCES, BETHESDA, MD

Thank you Chairman Brownback and members of the Subcommittee on East Asian and Pacific Affairs for the opportunity to present my views on malaria control.

Asia does not present us with the worst of malaria control problems; but this does not mean that there are no problems of malaria control in Asia. Conditions in many Asian countries are far worse today than they were decades ago when insecticides

were sprayed on house walls to combat malaria. The return of malaria to the countries of North Korea and South Korea is symbolic of the reversals that have occurred.[1] However the malaria problem in South Korea is much more than symbolic, 115,000 cases of malaria occurred in North Korea in 2001,[2] and malaria along the demilitarized zone now poses a risk to U.S. military personnel.

Today, the malaria control community around the world is locked into several different debates on best practices for dealing with continuing and, in some areas, worsening malaria problems.[3] One part of the debate is efficacy of different preventive measures, and this debate narrows to the issue of whether to use insecticide treated nets as the only preventive measure or whether to open the field to both the use of insecticide treated nets and indoor spraying of small quantities of insecticide on house walls. This is an important debate, because if the decision is to go with the former approach, then aid agencies will continue to use public funds to press countries to abandon their uses of indoor spraying to control malaria.

To gain a historical perspective, if we were to look from our 2004 vantage point back over the history of global strategies to control malaria, we would see a period of failure followed by a period of great success followed by a period of failure.

The first period covers the years before the mid-1940s. In this era, public health officials tried many methods of malaria control. Most of these methods failed, and malaria remained largely unabated. The second period, the era of intensive household spraying programs, came after the mid-1940s. Health officials sprayed small quantities of DDT on the interior walls of a house, a process known as indoor residual spraying (IRS). To contrast the small quantity on walls with agricultural usage, the amount used on just ten acres of cotton during a growing season would be sufficient for spraying enough houses to protect 4,500 people. Additionally, agricultural use puts the chemical directly into the environment and the food chain. When used in malaria control, the chemical is put only on house walls.

House spraying controlled malaria and even eradicated it in some regions. The period of spraying and its intensive control of malaria lasted for about 33 years, ending in 1979. In 1979, the World Health Organization strategy for malaria control changed to de-emphasize indoor spraying.[4] In 1985 WHO further distanced itself from indoor spraying in a World Health Assembly resolution (38.24) that directed countries to decentralize malaria control programs.[5] Those changes in global strategies brought most effective spraying programs to an end. Instead of spraying, WHO and donors like USAID place an emphasis on case treatment, community participation, and integrated vector management.[6] This modem strategy for malaria control has failed.[7] Since the startup of the "Roll Back Malaria" initiative in 1985, malaria rates have actually increased.[8]

In contrast to the results of WHO's current malaria control strategy, results with indoor spraying, and especially spraying with DDT, were spectacular. Almost without exception, when DDT was sprayed on interior house walls, it rapidly brought malaria rates down or completely eradicated the disease.

Just as the use of DDT in house spraying brought spectacular reductions in malaria, declining use of house spraying brought spectacular increases in malaria.[9] Data from countries of the Americas clearly document changes in malaria rates that coincide with changes in house spraying rates (Figure 1). Data[10] from Asian countries show similar relationships. Figures 2–5 contrast malaria rates in recent years with the years when DDT was used. The data represent annual parasite indexes (a population-based index of malaria prevalence) during the period from 1995–99

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[1] ProMed Notice "Malaria Reemerges-Korea," http://www.tmd.ac.jp/med/mzoo/ProMed/971118.html. Also: Ree, HI. Unstable vivax malaria in Korea. Korean J Parasitology 38(3):119–138.

[2] Malaria profile DPR Korea, http://w3.whosea.org/malaria/profile-dprk.htm.

[3] Attaran and Maharaj. Ethical debate: doctoring malaria, badly: the global campaign to ban DDT.BMJ. 2000 Dec 2; 321 (7273):1403–5.

[4] Seventeenth Report, WHO Expert Committee on Malaria. WHO Tech. Rep. Ser. No. 640 (1979).

[5] H. Gilles, D. Warrell, Bruce-Chwatts' essential malariology. Edward Arnold, Boston (1993).

[6] Implementation of the global malaria control strategy. WHO Tech. Rep. Ser. 1993, no. 839 (1993).

[7] http://www.rbm.who.int/amd2003/amr2003/chl.htm.

[8] G. Yamey. British Medical Journal: Roll Back Malaria: a failing global health campaign. 8 May 2004: http://www.accessmed-msf.org/prod/publications.asp?scntid=13520041552454&contenttype=PARA&.

[9] D. Roberts, et al., DDT, global strategies, and a malaria control crisis in South America. Emerg. Inf. Dis. 3:297 (1997). Also: Roberts, Manguin, Mouchet. 2000. DDT house spraying and re-emerging malaria. Lancet 356:330–332.

[10] Data presented in graphs were extracted from WHO reports: WHO, malaria profile: http://w3.whosea.org/malaria/pdf/ino.pdf.

compared with identical data from 1965–69. Differences in rates for the two performance periods are stunning.

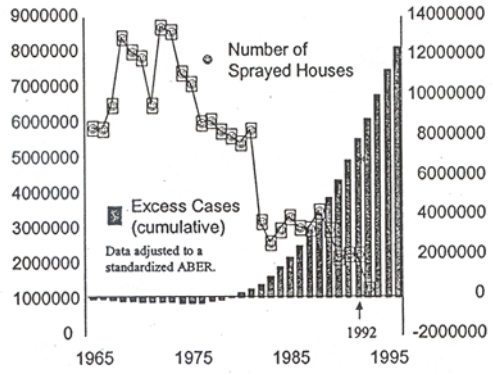
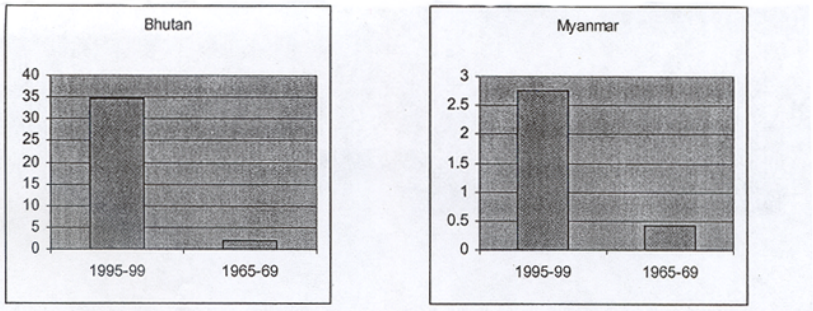


Figure 1. Impact of World Health Organization malaria control strategy in 1979 to de-emphasize indoor spraying of house walls and adoption of World Health Assembly resolution in 1985 to decentralize malaria control programs. Line graph represents numbers of sprayed houses. Bar graph represents cumulative numbers of excess cases over average numbers per annum for period 1965 to 1979. Left axis represents numbers of sprayed houses and right axis represents numbers of excess cases. Data presented for Brazil, Colombia, Peru, Ecuador and Venezuela. *First year number of excess cases grew by more than a million cases per year.[11]

Today, out of 30 countries in Asia, Bhutan, Myanmar, and Sri Lanka are the three most malarious.[12] In Bhutan, the malaria burden has grown 17.5-fold since the period when DDT was sprayed on house walls. For the countries of Myanmar, Sri Lanka, and India, malaria rates have grown 6.7-, 6.4-, and 807-fold, respectively.

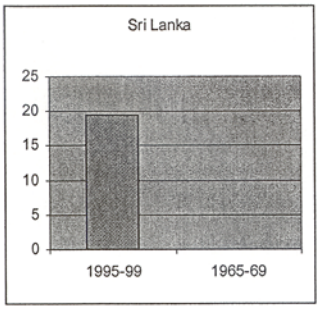


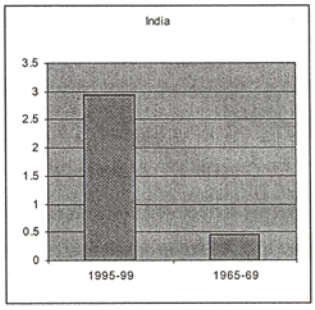
Figures 2 and 3. Annual parasite indexes (APIs) for Bhutan and Myanmar for comparison periods of 1995-99 versus 1965-59[13]. The latter (1965-69) covers a period when DDT was used to spray house walls for malaria control. The period 1995-99 represents a period when DDT was not used to spray houses. Left axes represent API values, or the number of cases per thousand population.

[11] Data extracted from: PAHO reports "Status of Malaria In the Americas." Calculations of numbers of cases derived by standardizing slide positive rates per 1000 population according to a standardized annual blood examination rate. Standardized rate was calculated as average for each country during period of 1965 to 1979. Adjustments were made for differences in size of population across 5 countries.

[12] Malaria rate by country: http://www.overpopulation.com/faq/health/infectious__diseases/malaria/asia.html.

[13] Data presented in graphs were extracted from WHO reports: WHO, malaria profile: http://w3.whosea.org/malaria/pdf/ino.pdf.





Figures 4 and 5. Annual parasite indexes (APIs) for Sri Lanka and India for comparison periods of 1995-99 versus 1965-59[14]. The latter (1965-69) covers a period when DDT was used to spray house walls for malaria control. The period 1995-99 represents a period when DDT was not used to spray houses (still used to a greatly reduced extent in India). Left axes represent API values, or the number of cases per thousand population.

WHO, however, touts one Asian country as a success story of its modem malaria control strategy, Vietnam. A WHO report[15] entitled "A Story to Be Shared: The Successful Fight Against Malaria in Vietnam" recounts the story of this success. The report describes Vietnam's transition from a program based on indoor spraying using DDT to a program of spraying with Icon (a pyrethroid) and treated nets, as well as changes in strategies of case detection and case treatment. If this is the success story that is the basis for USAID's and WHO's current strategies for malaria control, they need to re-evaluate the lessons this story teaches.

The story begins in 1991, when over a million cases of malaria occurred in Vietnam, and ends in 1999, when the number of cases of malaria dropped to under 400,000. The report's overview states that the government completely changed the malaria control strategy in 1991 away from use of DDT, implying that this was a voluntary change. In fact, I visited Vietnam's control program in the early 1990s. Government officials told me that they wanted to use DDT, because it still worked well in Vietnam, but Vietnam had long ago used most of its DDT stocks. The government had been trying to get DDT for several years. However international agencies and foreign donors refused to help the government make those purchases. Vietnam didn't choose to switch to another insecticide. It had no choice but to switch. I have heard this same story of international agencies and donors like USAID blocking use of DDT in country after country, in both Asia and the Americas.

Despite its unwilling switch, Vietnam did have significant reductions in malaria between 1991–1999, brought about by the use of indoor spraying, effective case treatment, and the use of treated nets. When indoor spraying is used, malaria cases drop immediately, which is fortunate as the use of nets grew slowly in Vietnam. The costs of the program however skyrocketed. In 1991, malaria control cost US$540,000. From then to 1999, the malaria program cost US$28 million (about US$3.5 million per year), and it didn't yield as large a decline in malaria cases as control programs had in the past. In earlier years when the country carried out DDT spraying, malaria declined by a factor of 20-fold (2000%) in the north and 4-fold in the south. In 1999, Vietnam reported 350,000 cases, representing a 2.9-fold decline from number of cases in 1991. In areas where malaria is brought under control, treated nets are the primary preventive measure. House spraying remains the primary means of control in remote areas, areas of persistent malaria, and in outbreak areas. Although Vietnam has enjoyed some success, the 350,000 cases in 1999 represents a lot of malaria, making Vietnam the fourth most malarious country in Asia.[16]

WHO and others seem to overlook the fact that effectiveness of the Vietnam system seems dependent on the authoritarian rule of a socialist system and its exten-

[14] Data presented in graphs were extracted from WHO reports: WHO, malaria profile: http://w3.whosea.org/malaria/pdf/ino.pdf.

[15] WHO WPRO. 2000. A Story to be Shared: The Successful Fight Against Malaria in Vietnam. l5pp.

[16] Malaria rate by country: http://www.overpopulation.com/faq/health/infectious__diseases/malaria/asia.html.

sive network of rural communes. The report states that once a year re-treatment of nets is not adequate and nets must be retreated every 6 months, which requires an extensive network of trained malaria control workers. Additionally, Vietnam workers declared in "final words of wisdom" that control requires a strong national program, one with a dedicated team, a high level of support and a fair amount of vertically controlled components. Ironically, WHO has worked diligently to eliminate the vertical components of malaria control programs, going so far as to direct countries to eliminate those infrastructures,[17] which Vietnam thinks were so critical to its success.

It is in fact quite peculiar that WHO and aid agencies such as USAID tout Vietnam's control effort as such a success story. The program bucks WHO policy in that house spraying remained a key part of control and the community participation, which WHO considers such a triumph, was not the result of the spontaneous embrace of the people, but rather directed by a strong centralized, authoritarian government.

Vietnam however is not the only country in Asia to control malaria. Thailand, a nearby country with similar vectors, environments, and malaria problems, has not embraced treated nets and community participation to the extent as has Vietnam. Indoor spraying remains, as it has for decades, the mainstay of Thailand's preventive measures. In 1999, out of the 30 Asian countries, Thailand was the 11th most malarious country in Asia; Vietnam was the 4th. Yet even though Thailand has similar conditions and far lower malaria rates [18] than Vietnam and has consistently maintained those lower rates for decades (see Figure 6, malaria rates for the comparison periods of 1995–99 and 1965–69), WHO and other aid agencies consider Vietnam the success story in Asia, not Thailand.

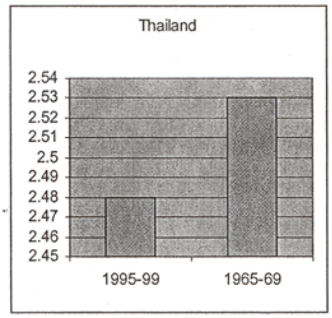


Figure 6. Annual parasite indexes (APIs) for Thailand for comparison periods of 1995-99 versus 1965-59. The latter (1965-69) represents a period when global eradication defined the methods of indoor spraying. The period 1995-99 is a period when indoor spraying was sustained, using DDT and other insecticides. Left axis represents API values, or the number of cases per thousand population.

Since the shift in malaria control policies that began in 1979 occurred, malaria has increased greatly in countries outside Africa (see Figures 1–5). In Africa, which had been excluded from the malaria eradication campaign of the l950s and 60s, there is almost no evidence that malaria rates are changing for the better as a result of implementing the WHO program of case treatment, community participation, integrated vector management, and treated nets, but not indoor spraying.[19] On the other hand, countries in Africa that have gone against WHO doctrine and used indoor spraying, such as Madagascar [20] and Zambia,[21] have seen large declines in malaria rates.

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[17] World Health Assembly adopted resolution 38.24 in 1985 calling on countries to decentralize their malaria control programs by moving malaria control into primary health care systems.

[18] WHO, malaria profile: http://w3.whosea.org/malaria/pdf/ino.pdf.

[19] G. Yamey. British Medical Journal: Roll Back Malaria: a failing global health campaign. 8 May 2004: http://www.accessmed-msf.org/prod/publications.asp?scntid=13520041552454 &contenttype=PARA&.

[20] Description of DDT use in Madagascar described on the Malaria Foundation International website: http://www.malaria.org/DDTEconomist14__XII__00.html.

[21] Sharp, et al. (2002), "Malaria control by residual insecticide spraying in Chingola and Chililabombwe, Copperbelt Province, Zambia" Tropical Medicine and International Health, 7, no. 9:732–36.

One fascinating aspect of attempts to implement WHO's current strategy for malaria control is that countries of Africa are the focal point of these efforts. This is doubtless due to Africa having the worst malaria problems in the world.[22] These countries were excluded from global eradication efforts and so have had limited experience successfully controlling their malaria problems. In this regard African nations are unlike many countries in the Americas and Asia that enjoyed high levels of success during the eradication era. Curiously countries that have had more experience with successful malaria control are less likely to adopt the use of treated nets. The Pan American Health Organization, for example, won't recommend them for malaria control in the Americas. Although donors provide generous funds for net use, nets are only now gaining a foothold in control programs outside Africa. As this occurs, the countries of Africa, frustrated by their continuing high malaria rates, are expressing interest in using indoor spraying.

As I stated at the beginning of this testimony, a large part of the debate about best practices for preventing malaria is whether to use insecticide treated nets as the only preventive measure or whether to open the field to both the use of insecticide treated nets and the indoor spraying of small quantities of insecticide on house walls. Frankly, I am surprised that we are having this debate at all. There is no scientific basis for stopping or preventing indoor spraying of insecticides. On the contrary, replacing spraying with nets defies a fundamental lesson of preventive medicine.

Clearly delineated within the annals of occupational preventive medicine is the fundamental truth that the least desirable preventive measure for reducing environmental risk is reliance on personal protective measures.[23] We have certainly learned this lesson over and over again in the military. This principle is expressed in the form of patients failing to take a full course of drugs, failure of troops to wear uniforms properly to prevent insects from biting, or failure to properly apply topical repellents, or failure to use their bednets.

It is a fundamental fact that proper use of nets requires user compliance. The user must be educated into proper use and must then be highly disciplined in proper use, night after night after night. Additionally, the user must be conscientious and follow a routine of repairing nets and retreating nets with insecticides. Another fundamental aspect of personal protective measure is that the measure may not lower overall environmental risk. For example, placing infants or pregnant women under treated nets may do little to lower risk for others in the household. For these reasons, even if we were certain of full user compliance, we would still need to be certain the practice would truly deliver a meaningful level of disease prevention. This is an important question, and I will present one single study to illustrate why we should worry about that specific issue opposed to blanket acceptance of treated nets as the only approach to malaria prevention.

A bednet study was conducted in the small and highly malarious Phan Tien village in southern Vietnam from 1995 to 1999.[24] Case treatment and treated net use was closely supervised and tightly monitored. Malaria was reduced, but, as stated by the investigators, "The number of passive cases [cases coming to the clinic for diagnosis and treatment] had dropped steadily from year to year (despite an increase in population), but rose again in 1999." The investigators also stated "After 1997, when malaria incidence had started to decline, the population became less interested in participating." This is a very telling statement that confirms the weakness of methods that require sustained user compliance. My summary of this study is that at the beginning in 1995 there were 104 cases of falciparum malaria, in the last year of the study, in 1999, there were 102 cases. So, after five years of costly effort, there had been a 2 percent drop in falciparum malaria, a difference of 104 cases versus 102.

To iterate, the fundamental lessons of occupational preventive medicine is that use of personal protective measures is the least desirable of methods for reducing environmental risk. The flip side of this principle is that the most desirable method for reducing environmental risk is to engineer risk out of the human environment.[25]

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[22] Ranking of countries by malaria mortality: http://www.overpopulation.com/faq/health/infectious_diseases/malaria/asia.html.

[23] Rom, WN. Editor. Environmental and Occupational Medicine, Third Edition. Lippincott-Raven Publishers, Philadelphia, PA:1753–1755. Also: Olishifaki, JB, Editor-in-Chief. Fundamental of Industrial Hygiene, Second Edition. National Safety Council. Section on Fundamental Concepts, pages 35–39.

[24] Hung, LQ, et al., Control of malaria: a successful experience from Vietnam. Bulletin of the World Health Organization 2002;80:660–666.

[25] Rom, WN. Editor. Environmental and Occupational Medicine, Third Edition. Lippincott-Raven Publishers, Philadelphia, PA:1753–1755. Also: Olishifaki, JB, Editor-in-Chief. Funda-

The use of indoor spraying is absolutely consistent with that fundamental principle of preventive medicine. Let me explain why.

Most cases of malaria are acquired inside houses. Mosquitoes that aggressively enter and bite indoors transmit the infections. Indoor residual spraying can act to prevent mosquitoes from entering houses in the first place. If they still enter, then chemical contact indoors may stimulate mosquitoes to exit without biting, or if they remain indoors, the chemical can, with longer contact, kill the mosquitoes. In other words, the chemical applied to house walls exerts multiple and sequential actions to prevent indoor transmission of malaria and other diseases.[26]

These relationships explain why indoor spraying has been so wonderfully effective in combating malaria and other diseases. I want to emphasize that lack of effectiveness is not the reason that WHO and bilateral and multilateral donors have pressed countries to stop indoor spraying. To the contrary, indoor spraying has been and continues to be the most highly effective measure yet discovered for malaria prevention. WHO, USAID and others argue that indoor spraying should not be used because it requires a strong and well-developed public health infrastructure. This is a contrived argument that ignores the lessons from the history of malaria control. House spraying was used to dramatically reduce malaria in many countries of the world long before WHO defined the organizational structures for malaria eradication by use of indoor spraying. The countries accomplished those great achievements largely on their own accord. I can think of two remarkable examples, one is Guyana and another is Taiwan. Guyana began experimenting with indoor spraying in 1946. The country quickly instituted a national program of indoor spraying and reduced malaria by 99 percent within 3 years.[27] Taiwan began a national program in 1952 and had reduced numbers of cases from 1.2 million per year to just 676 in 1956.[28] These accomplishments predated the beginning of malaria eradication. In comparison, during the last 20 years treated nets have been pilot tested in many countries. There is not one result that is even remotely comparable with the performance of indoor spraying in Guyana or Taiwan.

The infrastructure argument against indoor spraying also ignores the fact that WHO, bilateral, and multilateral agencies have implemented policies and strategies under a 1985 WHA resolution that have effectively eliminated infrastructures they claim are needed for indoor spraying. So it is extremely disingenuous to say a method cannot be used because infrastructure does not exist, when those who oppose using the method are directly responsible for eliminating the needed infrastructures in the first place.

What I have described in the preceding text and figures is a struggle between public health science and an environmental ideology. It is an ideology that strives for an environmental utopia, an environment free of man-made chemicals. The ideology is strong, pervasive and extremely destructive. It prioritizes a scientifically unfounded risk of environmental harm over the basic health needs of the world's poorest and most vulnerable people. As the driving force behind the modern policies for malaria control, it ignores the time honored practice of malaria control to use all available measures to curb the disease, and replaces it instead with partial control measures adopted because they are apparently more palatable to those living in developed countries. Our national and international bureaucracies put this ideology over the needs of poor people in developing countries. I, along with many others in the malaria control community, do not agree with this ideology. This ideology has created a colossal public health and humanitarian disaster. In particular, we object to the use of public funds to pressure developing countries to comply with policies and strategies that increase the risk of disease and death. It is an irrefutable fact that for over two decades WHO, bilateral and multilateral donors, and other international agencies have been pressing countries to abandon indoor spray programs. The world has already paid an enormous price in lost life, lost economic vitality, and lost human welfare as a result of those practices. It is time to stop this flagrant use of public funds to force compliance with a scientifically fraudulent and immoral ideology.

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mental of Industrial Hygiene, Second Edition. National Safety Council. Section on Fundamental Concepts, pages 35–39.

[26] Roberts, DR, et al., 2000. A probability model of vector behavior: Effects of DDT repellency, irritancy and toxicity in malaria control. J. Vector Ecol. 25(l):48–61.

[27] Giglioli, G. 1951. Eradication of Anopheles darlingi from the inhabited areas of British Guiana by DDT residual spraying. J. National Mal. Soc. 10:142–161.

[28] Department of Health, Republic of China, Malaria eradication in Taiwan (Department of Health, Republic of China), p. 183.

Senator BROWNBACK. Thank you, Dr. Roberts. I look forward to questioning.

Dr. Desowitz, thank you for being here and your years of service. In reading your resume and background, that is quite impressive.

STATEMENT OF DR. ROBERT DESOWITZ, ADJUNCT PROFESSOR OF EPIDEMIOLOGY, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, NC

Dr. DESOWITZ. Thank you, Senator Brownback. Welcome to our magic circle of malariologists. [Laughter.]

I think everything I wanted to say has already been said, but I will begin with the conventional malariological plea that there is a carnage every year of 2 million to 3 million children and pregnant women. This is usually followed by "send more money."

I would depart from that in expressing my feeling that for the last 50 years, no child, no pregnant woman, no transmigrant need have died of malaria. We disparage the pharmaceutical industry for not being attentive to Third World needs, but in actual fact we have had therapeutic drugs that could cure each and every malarious person, again for the last 50 years, or if you want to look in the longer perspective, practically for the last 400 years, with quinine always being the bulwark.

Today, there is present a number of therapies that act quickly, they act effectively, and they will act against multidrug-resistant strains of falciparum, the killer malaria. Foremost of those drugs is Coartem. This is a modern drug that is 2,000 years old, as you know. It is an extract of Artemisia annua, the sweet wormwood; China, I think first used for hemorrhoids 2,000 years ago, but it seems to be better for malaria. [Laughter.]

It is produced extensively in China.

A late-night thought occurred to me that—I think it was in part of the debate the other night where they were talking about Afghanistan and opium poppy growing—Artemisia would be a marvelous replacement crop for that.

Senator BROWNBACK. There is a good idea.

Dr. DESOWITZ. Actually there is only one drug that is being used now, and this is a drug put together by Novartis. It is called Coartem and it is a combination of artemisinin, which acts very quickly but has a very short half-life, and a drug called lumefantrine, which is terrific. It sort of mops up the rest of the parasites. Coartem, as far as I know, is the only one of the combined artemisinin therapeutics that is commercially available and standardized. It is produced by Novartis.

Now, Novartis is selling Coartem. If you go to your friendly Swiss drugstore, it is $52. You might get it at your friendly Swiss Wal-Mart, if there is such a thing, for maybe $30.

At a consultative meeting that I attended last year—I think it was last year—Novartis was trying to introduce Coartem into Africa. They said we have enough of the drug—in fact, they gave us these things, ballpoint pens and a little thing as they sell it. It is a beautiful packaging for the whole therapy. They said, yes, we sell it for $50, but we will give it to Africa for our manufacturing costs, which was 90 cents which, to a naive person like myself, was a

rather startling insight into the pharmaceutical industry. Where that is going I am not sure.

In June of this year, I had the privilege and delight to be faculty at American Fogarty-sponsored, along with the Gates Foundation, workshop in Tanzania on malaria pregnancy. We had 21 young Africans, a third women, Ph.D.s, physicians, terrific kids, who gave great hope for Africa, along with one of the great African men himself, Dr. Mutabingwa, as faculty. They have found and declared that Coartem is the only thing that works. We had been trying to peddle artemisinin plus amodiaquine, which was sort of a chloroquine. It has not worked. They are going completely to Coartem now. West Africans are a little more uncertain about this, but they are coming around to it as well.

The question is: Can we get Coartem to the Africans? Can we get Coartem and we diminish the malaria problem in Southeast Asia, but it is growing and it is terrible. Areas on the Burma—thank you, Ms. French, for telling me it is still Burma because I never know how to spell Myanmar—on the Burmese-Thai border. In Cambodia it is a tremendous problem. They have had outbreaks, pitiful outbreaks even in India again. Asia is feeling a real brunt again of malaria. We do not know what is happening in the fertile crescent called Iraq, but that used to be a terribly malarious area.

Whether USAID directly can buy a drug that is not approved by FDA I do not know. Whether other arrangements—Novartis have no desire whatsoever to license this in the United States, but it is approved by the European Union, their equivalent of FDA.

So, for the moment, with falciparum malaria, I think we have to go with Coartem. At $1, people object. They say it is too expensive. It is inconceivable to me that we would allow a child to die for what would cost us a bottle of aspirin at a discount store.

There are other drugs, malarone, mefloquine, which is losing its effectiveness, but we do have backup drugs.

Nobody has to die. I put to you, I think we have the money. Everybody decries that there is not enough funds. You put it all together and there is enough funding to save every child if we can get the drugs to them.

Let me depart from that a bit and let me speak to DDT. The passions are running very, very high once again and always excited since St. Rachel wrote her book. It has produced some of the most violent discourse I have ever heard. I will tell you a story about Alan Ginsburg, which is in the book, going down University King Street when he had a very drunken evening with us actually saying, I am the bald eagle, when I was trying to describe the effect of DDT on him.

But it is coming back. We have just had a very productive meeting last month, Don? July. Time passes. From the National Academy of Sciences on DDT, which they now tell me that there is not going to be any report forthcoming because NAS is beginning to feel the heat.

I have always been a great advocate of DDT. It is a unique drug. It is the best thing since sliced bread. It is terrific. There is nothing like it. My concern is that in our fervor to reintroduce it, we may overstate the case.

Don, who is a card-carrying entomologist, knows more than I do about it. But I was taught that there are about 50 or 60 anopheline vectors of malaria and each one of them has characteristics that are genetically ingrained and they carry their genetic behavior out like a 2-year-old kid. Some of them will fly indoors, some will bite indoors, some will bite outdoors. They will have different feeding preferences.

In the fifties and sixties, when they were formulating the great global eradication of malaria, which we put $800 million into in 1960 dollars, which was neither global nor eradicating, we had great intelligence at that point. We knew where to use DDT, how to spray it, and where to spray it. And DDT, as we have seen, particularly used with Coartem—Coartem I might mention also kills the stage of the malaria parasite which is transmitted through the mosquitoes. So there is a synergistic effect, and that is why it was so effective. And it is a unique drug.

But what we are lacking today—again, if I might say sort of a rye joke of age, but the only thing the global eradication scheme eradicated was the malariologists. The malaria did fine. And I do not think we have the intelligence today to be able to pinpoint exactly where and how we must use DDT. I think somehow we must gain this even if it means—sorry—taking the money from vaccine researchers.

In this last month or so or 2 months, I have been surprised and rather amazed by the, again, various strong feelings on the USAID program. Again, I suggested in my report that what I think is needed for the general intelligence of where we are going to go and what we are going to do, is an independent body of people, completely independent, to try to sort out what they are doing, how they are doing, and what the malaria situation is today. Some of those people are still around. We could still do it and they are still independent.

[The prepared statement of Dr. Desowitz follows:]

PREPARED STATEMENT OF ROBERT DESOWITZ, PHD., D.SC., EMERITUS PROFESSOR OF TROPICAL MEDICINE AND MEDICAL MICROBIOLOGY, UNIVERSITY OF HAWAII; ADJUNCT PROFESSOR OF EPIDEMIOLOGY, UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, NC

The manner in which an industrialized nation comes to the assistance of the tropical third world's health problems is a faithful representation of its economic and diplomatic policies. It is also a reflection of its moral and ethical values. In turn, malaria has traditionally been the "epidemiological metaphor" to analyze and assess donor health programs and strategies. But malaria, especially in its most lethal guise caused by *Plasmodium falciparum* is more than a metaphor. It is estimated to kill between 2 and 3 million each year; young children and pregnant women being its chief victims. It is a major cause in hyperendemic regions of spontaneous abortion and low birth weight babies. Billions of tropical and subtropical peoples are at risk, hundreds of millions are infected. Even in its non-lethal form, caused by *Plasmodium vivax,* it is responsible for untold sickness with the debilities of anemia and recurrent fevers. Populations burdened with malaria suffer from the lethargy and cognitive defects that inhibit economic, technological and cultural progress.

Our country has had a long, and continuing interest in malaria. First, because of our epidemiologic history in which from about 1542 to 1942 we have been a "tropical" country with entrenched "tropical diseases." Malaria, which in my 1995 Gorgas Memorial Lecture at the National Institutes of Health I characterized as being "as American as the heart attack," was entrenched in a vast zone between Florida and New York. Second, malaria has been a major factor in the prosecution of our tropical wars with, for example, as many troops in Vietnam being disabled from combat by malaria as by the wounds of war. The military has responded since the 1940s

through their medical research establishments at home and abroad which continue to be highly productive. The Army, at Walter Reed Army Institute of Research with its satellite laboratories in endemic sites such as Thailand, Kenya, and Malaysia. The Navy at its Medical Research Center in Bethesda and satellite units in Egypt and Indonesia. I would particularly note the military's contributions to medical entomology and discoveries of new antimalarial therapies.

In the civilian research arena the National Institutes of Health's Malaria and Parasitic Diseases Laboratories are internationally renowned for their basic research on the malaria parasites. There has also been a long and large body of federally funded research coming from universities and institutions. The Center for Diseases Control have continuing activities in malaria, their great strength being epidemiological and operational studies in endemic settings. There have also been American organizations to promote the public understanding of malaria and facilitate interchange of ideas and knowledge between malaria researchers throughout the world. The Malaria Foundation International, based in Atlanta with its founder Dr. Mary Galinski of Emory University at the helm is the most notable organization and has the great potential ability to be a non-biased, non-government instrument to organize working parties for strategy sessions. More recently the Bill Gates Foundation is funding malaria projects with a generosity reminiscent of the Rockefeller Sanitary Commission and Foundation of the early 20th century.

Our government has also had a long history of contributing to international malaria endeavors. There is the $800 million, in 1960–1970 dollars, we gave to the World Health Organization for their Global Eradication of Malaria program—that was neither global nor eradicating. The international malaria activities of our own Agency for International Development is now, quite properly, under scrutiny by this and other congressional committees. It is estimated that the USAID annual budget for malaria is $85 million. In addition, since 1972 when USAID embarked on their malaria vaccine project I estimate a further $250 million has been spent. The project has produced 5 convictions for criminal felonies but no vaccine.

It is the inherent nature of the scientific establishment to complain that there is never enough money to make the progress they envision to bestow the benefits of research on suffering humanity. Malariologists, basic "molecular" laboratory-based researchers and applied "field hands" alike are given to much hand wringing and in supplicating for more funding invariably citing the 2–3 million annual malaria death rate. From my now comfortable position of retirement—free at last from grant writing, I would offer the, no doubt challengeable, opinion that the total monies, from American and international sources are adequate to bring the malaria carnage to an end. That malaria is an eminently treatable disease and no child, born and unborn, no pregnant woman, no non-immune adult transmigrant need suffer or die of malaria.

1. Prevention, let alone eradication, is problematic. There are the means to reduce transmission, notably DDT and insecticide-treated bednets which I will speak to later. Priority should be to furnish and deploy appropriate, effective antimalarial chemotherapy in the endemic areas of South/SE Asia (as well as in Africa and other regions such as Melanesia).

The cheap, former sheet-anchor of antimalarial therapy and prophylaxis, chloroquine, is now virtually useless, because of parasite multi-drug-resistant strains of *Plasmodium falciparum* and to a growing extent against *Plasmodium vivax.* Furnishing of chloroquine by donor agencies is useless—and dangerous. Childhood mortality can rise as much as eleven-fold when it is not replaced. Until recently the Global Fund on the advice of the WHO representatives in Africa (and elsewhere?) were still buying chloroquine to distribute to the health services of sub-Saharan nations. The overall and nation-specific antimalarial drug policy(s), if any, of USAID must be scrutinized by unaffiliated experts as expeditiously as possible.

The antimalarial of choice is the artemisinin combined therapeutic (ACT) Coartem (artemisinin+lumefantrine) which rapidly resolves parasitemia and fever in severe, multi-drug-resistant falciparum malaria. It also has the unique property of acting against the gametocytes (the stages responsible for transmission through the Anopheles mosquitoes) and thus has a useful transmission-lowering action, especially when used in conjunction with DDT spraying. Most sub-Saharan African nations have now designated Coartem as the antimalarial of national policy and its purchase is being funded by the Global Fund and other donor agencies. Coartem is also being used, to an increasing degree, in SE Asia, especially in the hyperendemic areas of the Thai-Myanmar border, Cambodia, Vietnam and Laos. It is essential that USAID adhere to and support these national policies for Coartem's use in the

treatment of falciparum malaria.[1] Recent work by Dr. Francois Nosten and his colleagues on treating pregnant women in the unstable situation on the Thai-Burma border indicates that Coartem is safe when used to treat malaria of pregnancy. Coartem is relatively expensive but the day of the 10 cents chloroquine treatment is over—gone! finished!—and I believe no American would deny a child to his or her life for what would be the cost a bottle of aspirin.

2. DDT has once again returned to become once again a contentious issue as an anti-malarial strategy. A product of World War II research (in Switzerland) it remains the unique insecticide by virtue of its long residual (up to 6 months) activity, its safety for humans, and its dirt-cheapness.

There is now a coterie of American scientists and science journalists who are vigorously advocating—demanding—that DDT be returned to the antimalarial armamentarium. Indeed, countries such as Ethiopia and South Africa have effectively deployed DDT to combat recent malaria epidemics. Several months ago the National Academy of Sciences/Institute of Medicine convened a meeting to reconsider the introduction of DDT. A report of the meeting has not been forthcoming and may never be forthcoming as the NAS feels the heat from the "Silent Springers." At that meeting I voiced my belief that DDT is incomparably useful—where it is useful. And I voiced my concern that the new combative passion for DDT may unrealistically overstate the case. An axiom of malaria control is that each of the 50, or so, Anopheles species that are malaria vectors has genetically determined characteristics (biting preferences, breeding-water preferences, post-feeding behaviors, insecticide resistence) that make it a target or non-target for attack by DDT. A wry "in" joke amongst the surviving "field hands" malariologists is that the only thing the WHO global malaria eradication program eradicated was the malariologists. A real problem, as I see it, is that we do not have the contemporary epidemiological/entomological intelligence from this absent/diminished expertise to formulate region-specific logical strategies for malaria control.

3. Insecticide treated nets (ITNs) are a favorite antimalarial strategy of donors. They are easy to buy, easy to distribute (for free). Pilot studies have resulted in a 30 percent reduction in malaria-caused mortality. Other pilot studies have shown little or no effect and a few studies, mortality has actually risen. Going against convention I would give ITNs lower priority for funding if it competes with chemotherapeutic needs.

4. Again, contrary to fashionable molecular frontier malariology I offer my opinion that the much heralded malaria vaccine is a goal, an illusion, that has not been realized and may never be realized in combating the disease at a population level.

Research on the vaccine has been pursued for over 70 years with increasing intensification of the effort during the past 30 years. Hundreds of millions of dollars, the energies and resources of some of our best scientific minds have been, and are, devoted to vaccine research. It would be appropriate to now reexamine the overall malaria vaccine programs and determine whether some of those resources, intellectual and financial, should be redirected to applied malariology.

Some recommendations for the committee's consideration:

1. We urgently need an independent American panel of experienced malaria experts who can speak with authority to authority (this committee?).

2. The panel should have a relatively long term working life, probably over several years and be funded for their various investigatory and administrative needs. There was such an assemblage in the early 1970s, the Effect of Herbicides in Vietnam Committee (in which I headed the epidemiological investigations) under the administration of the National Academies of Sciences and funded by Congress that worked very well. The malaria panel could similarly be organized by, and work under NAS, possibly in collaboration with the Malaria Foundation.

3. The panel should critically examine American malaria programs and American programs that interface with international programs such as the WHO Roll Back Malaria. This is especially true in respect of USAID's malaria, funding, policies and activities. The panel would therefore need authority to speak with USAID personnel within the United States and at their overseas postings, and have access to their records (much in the manner that the herbicide committee had in respect to military personnel and their spraying records).

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[1] Coartem is the only ACT formulation that is produced commercially. It is an approved drug in Europe but Novartis has no intention of seeking FDA approval in the United States (can USAID directly or indirectly purchase a FDA unapproved drug for overseas distribution?). The Coartem treatment pack of 24 tablets sells for $30 to $50 in Europe; however at the 2003 consultative meeting, which I attended, called by Novartis, the company declared that as a responsible global industrial citizen they would sell it to Africa at their manufacturing cost—$1.

4. The current lack of good malaria-entomological intelligence should be addressed by the panel and have the funding to act on this. The appropriate experts of the panel (and the experts they would need to co-opt) should be able to obtain country-by-country inventory on vectors, their behaviors, and suitability for attack by DDT as well as the suitability of ITN distribution.

5. USAID should carefully consider, if not be obliged to follow, the expert panel's finding and decisions—especially in respect of chemotherapeutic and DDT deployments. There should be a reevaluation of United States obligations and interactions with international bodies, notably the WHO, on the basis of the panel's findings.

6. The guiding principle of America's malaria activities should be to save lives as expeditiously as possible—to drug malaria into submission, to end the carnage of the young and pregnant in the malaria regions.

Senator BROWNBACK. Dr. Desowitz, let me make sure I understand this point. You are talking about, I guess, a global malaria survey. Am I understanding you correctly?

Dr. DESOWITZ. Yes.

Senator BROWNBACK. Of both cases and vectors.

Dr. DESOWITZ. Cases and vectors. We must know where the cases are, what they are responding to, what the vectors are, and as we knew in the fifties, what their behavior is. Are they still DDT-resistant? It may be foolish to spray in some areas. I do not know. I do not think anybody else does now. We did 50 years ago, but we do not now.

Senator BROWNBACK. Why did we know it 50 years ago and we do not know it now?

Dr. DESOWITZ. We went at this like gangbusters, sir. In 1955 when they were beginning the global eradication scheme, there were extremely well-trained entomologists and malariologists. The whole idea, then, was to carefully evaluate all the vectors and to carefully evaluate the epidemiology. They did not always act on that knowledge because it became very politicized, but it was there. If we had that knowledge today, I think we would be in a much better position and we would not have to be arguing with each other as well.

Senator BROWNBACK. Dr. Roberts, what do you think of the survey? Do you believe we need that today?

Dr. ROBERTS. I do believe we need more medical intelligence on a variety of issues in this regard. I think, for example, we do not have a really good handle on how bednets, for example, actually work and how the different insecticides in these bednets actually work. But if we had a good handle on that and we had good intelligence on vectors and vector behaviors and vector susceptibilities to insecticides in various regions, it would certainly be beneficial. However, I do believe we have the tools.

I would also like to emphasize that we are not really talking about going back to the silver bullet days of just DDT. The struggle is not that. The struggle is to be able to use it at all. I think if we could use all of the tools that we have available today, they will work in one configuration or another in practically any place in the world. That is just my opinion.

Senator BROWNBACK. Dr. Desowitz, you made a very bold statement that there is no child, no woman, no person in this world that should have died of malaria over the past—did you say 50 years?

Dr. DESOWITZ. Yes.

Senator BROWNBACK. That must make you terribly frustrated to see these numbers go up then. I mean, if you are saying that 50

years ago nobody should have died—we are in 2004 and you still have a million annual deaths from malaria.

Dr. DESOWITZ. Yes. The simple fact is that each and every case of malaria, if you got to it in time or you had proper medical administration, is and was treatable. If you did not get the drugs, if you faked the drugs, if you sold the drugs, if you purloined the drugs, or if you did not have the administrative infrastructure to get the drugs to the people, that is another thing again. But the drugs were there. Malaria was always treatable.

Senator BROWNBACK. Dr. Roberts, I have received reports from individuals, not just on DDT, saying that the U.S. Government is pushing some ineffective drugs. Not that they are counterfeit or poorly made drugs, but they are just ineffective drug regimes that we are supporting. Have you heard that? Is there any accuracy to these reports?

Dr. ROBERTS. I have heard that. I think there is some documentation for that. I believe there was an article published in the Lancet not too long ago that would document that that indeed is occurring. But to be honest with you, sir, I am not an expert in the area of drugs for malaria control.

Senator BROWNBACK. Dr. Desowitz, have you heard this charge?

Dr. DESOWITZ. I have correspondence from many parts of the world on this. And I do not know. I do not know whether it is true or not true.

Senator BROWNBACK. Are there ineffective drug regimes out there that are being pushed by governmental entities?

Dr. DESOWITZ. Up until a year ago, they were still pushing chloroquine. It was a kind of a chloroquine addiction. They were killing people with this. Who was buying it? Certainly WHO was pushing it. The Fansidar kind of combination was being used and it again was useless in many places. But the Global Fund, as I understand it, was buying it.

Now, I think, they have seen the justice in it and they are going to the artemisinin combinations. Whether they are going to the only effective one I do not know, and I do not know whether Novartis will be selling it to Asian governments with the same concessionary price. I do not know.

Senator BROWNBACK. Dr. Peterson, you have been very kind to stay through this, and I appreciate that. May I invite you back up to the table? Is there any response you would care to give to these two expert witnesses? I would like to give you that chance so that we have your response to some of the input from these experts, as we try to formulate the right answers and the sort of policy issues to put forward.

Dr. PETERSON. Thank you very much, Senator. I appreciate the chance to respond.

First, let me say, I think they are both correct that during the eradication effort of the fifties and sixties, the thing that died was the malaria expertise. We do not have the entomologists and the malariologists that we used to have when there was such a huge push, when it was really the single, big public health endeavor that was happening at that time.

We have been tracking the drug resistance in doing the surveillance for where drugs are working and where they are not working.

That is a lot of what you will see, when we do the breakdown, that we have been spending our money to be able to track how fast it is moving, where, and which are the priority countries to try and get the artemisinin drugs into.

We have good entomologists and good malaria folks at CDC, but there are few. I have worked in that branch at CDC, but there is not a lot there. I did a little consultation, and my understanding is that we probably do not have the world mapped out to the extent that we did in the fifties or sixties as far as the mosquito vectors, which ones are still transmitting malaria of all of the different kinds, which ones are still resistant to DDT, and which ones are not resistant. So there are some holes that could be fixed and some expertise that we need to have.

On the drugs, we are moving to the combination therapy, and together with the surveillance work, we have been pushing very hard for moving countries. We have actively helped specific countries, as they have shown that they have got significant resistance, to be some of the first ones to move to the combination therapy.

I am not sure if Coartem, the Novartis product, is the only effective one. That is probably something we need to look at. We are sure that we need to be working and bringing countries to combination therapies and that one of the combinations should probably be the artemisinin.

It is wonderful that Novartis is willing to provide for Africa, but it always better if you have multiple providers. Right now, China is the only place that is growing the artemisinin, and Novartis is really the sole provider of the Coartem.

What we would like to do is to broaden that. I do not know if it has been tried in Afghanistan. I have seen and been in the poppy fields myself, and we would love to see them growing something different, I promise.

We have been working in Tanzania and in Ethiopia so that Africa can begin to grow the drug that is needed for its own malaria. That would bring income to Africa and then they would have the solution to their malaria problem in their own countries. So that is part of what we have been trying to move forward so that there will be an adequate supply of the drug as we expand the capability of responding with the combination therapies.

Senator BROWNBACK. Dr. Peterson, what about Dr. Roberts' comment about the Vietnamese study on bednets? When you were presenting—or was it you or Dr. Desowitz—the 5-year study that showed that at the end of the 5 years you did not have any significant difference in malaria infections. In my experience I have run a little agency that supervised insecticides in the State of Kansas. I had entomologists working in the agency. Just the idea that you are going to be surrounded by mosquitoes and if you stay under the bednets, you will be all right, and if you get out you are not, seems like a really crazy strategy to me. What if, in the middle of the night, you have to do something. You are not going to take the bednet with you and in that system you would subject yourself to exposure to the mosquitoes. This does not seem to me that this system works over a period of time. Yet, it is where we are putting, it appears, most of our effort.

Dr. PETERSON. We are putting a fair amount of effort there. We do have studies that show that they do work. In fact, with the malaria bednets, you do not even have to get as high a community coverage as you do for indoor residual spraying. If you do community spraying with the indoor residual spraying, in order to get collateral benefit, you have to cover 80 percent of the homes in that community. With bednets, if you have them in a community—and we have got studies that have shown this—you not only protect the person who is under the bednet, you begin to protect others in the household who are——

Senator BROWNBACK. How?

Dr. PETERSON. Because it does kill the mosquitoes that land on the net. It is some of the same kind of things that he talked about for indoor residual spraying, but you have to get a higher coverage in the community with the indoor residual spraying.

The doctor talked about the——

Senator BROWNBACK. Dr. Roberts, respond to that, would you please?

Dr. ROBERTS. Actually, I do not agree with that assessment at all. It really comes down to some very basic relationships. If a house is sprayed, the residents of that house are protected. If an individual is inside of a bednet, that individual inside the bednet is protected. For the bednets, we use pyrethroids. For indoor residual spraying, we have in the past, at least, used DDT. DDT is the most potent spatial repellent we have yet tested.

The pyrethroids exert no spatial repellent action. They are powerful contact irritants and they are potent toxins, but they exert no spatial repellency action at all. And that separates them from DDT. If you sprayed a house wall with the pyrethroid, the mosquitoes will enter. We know that. We have tested it in the field. We have tested it in the laboratory. When the mosquitoes enter the house, they will bite. The pyrethroid is a powerful locomotor stimulant, and so in some cases, it could even increase the biting because they are agitated. They are highly agitated. With DDT, they will not enter the house.

So there are major, major differences between modes of action of these chemicals. And, of course, as you commented on, there are differences in the way they are being used.

Senator BROWNBACK. Plus, it just seemed to me that instead of having individual protection, you try to expand your sphere so that people within the sphere are protected—that seems to make a lot of sense to me.

Dr. PETERSON. I agree it does make sense, and in fact, that is part of what we have seen with the bednets. They are a protection also for people who are not covered by the bednets. We can get the studies for you.

[The information requested was submitted and has been made part of the committee's permanent record.]

In outbreak situations, there have been a number of times when we have provided both strategies in a household, both the spraying of the walls and the bednets around the individual person, and that combination is very effective.

Senator BROWNBACK. And that is great. Let us keep going that way.

Dr. PETERSON. I think that is my major point, that we have two modalities that provide protection. We need to try and use both.

Senator BROWNBACK. That is my major point. I see you funding one, but not the other.

Dr. PETERSON. We are both providing bednets and trying to build the capacity of the local systems themselves to produce and to distribute the bednets.

Senator BROWNBACK. OK, not spraying or using DDT.

Dr. PETERSON. We are equivalently encouraging the systems to provide the DDT as well.

Senator BROWNBACK. I do not understand the hesitancy to use DDT other than the really strong philosophy and difficulty you might encounter from some people on the use of DDT. I understand that, I understand that completely. But I do not understand why there would be any hesitancy to using or supplying DDT other than, I understand, a strong pushback from the environmental community or others that do not like DDT. I do not like it at all. I have seen that war and I understand that philosophical position and I respect it, but as somebody who is trying to pay for treatments, I do not understand why you would not be using DDT.

Dr. PETERSON. We have no opposition, and in fact, through the Global Fund and other moneys, we are supporting it and we are supporting programs that have incorporated it.

I think, again, there are rural areas where it is going to be harder to reach, and the doctor talked about the compliance, the staying under the bednet. We have equivalent situations with people willing to have their homes sprayed with insecticides, but not liking the color that it changes it and repainting it. We have compliance issues in all of these areas, and therefore, we need to have both available in the places where it is most appropriate.

Senator BROWNBACK. I agree with that.

Thank you. Thank you, gentlemen, for being here, for your years of work and expertise and effort. I look forward to the day when that number starts going way down. Maybe we do not get to zero soon, but we really start to drive those numbers down hard and fast. I do think it is within our capacity to do it. Thank you all for being here.

The hearing is adjourned.

[Whereupon, at 4:05 p.m., the subcommittee was adjourned.]